VOLUME 40 NUMBER 5, PART I NOVEMBER, 1955

AMERICAN JOURNAL OF OPHTHALMOLOGY

THIRD SERIES FOUNDED BY EDWARD JACKSON

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DEPARTMENTS

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1. Am. J. Ophth. *38*:576 (Oct.) 1954.
2. Brit. J. Ophth. *39*:109 (Feb.) 1955.
3. Canad. Anaesth. Soc. J. *2*:191 (Apr.) 1955.
4. Brit. M. J. *1*:1457 (June 18) 1955.

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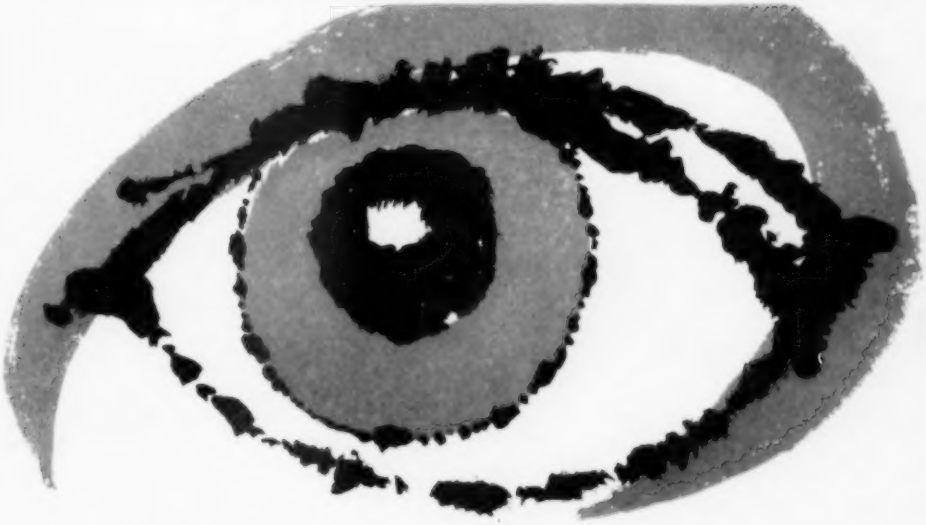

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AMERICAN JOURNAL OF OPHTHALMOLOGY

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AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 40 NOVEMBER, 1955 NUMBER 5, PART I

PRIMARY DEGENERATION IN THE VICINITY OF THE CHAMBER ANGLE*

AS AN ETIOLOGIC FACTOR IN WIDE-ANGLE GLAUCOMA

C. C. TENG, M.D., R. T. PATON, M.D., AND H. M. KATZIN, M.D.
New York

Present knowledge of the cause of wide-angle glaucoma is based on a series of findings in three categories of clinical investigations: gonioscopy, tonography, and aqueous-vein studies. These findings have been mutually consistent, for the most part, and have tended to emphasize the fact that this type of glaucoma is due to blockage somewhere in the chamber angle.

Progress in the study of the pathogenesis, however, lagged behind the clinical work. This is mainly because chronic simple glaucoma rarely requires enucleation in its early stages and in later cases, when enucleation is necessary, secondary changes predominate, submerging the early changes. It is of little use, therefore, to study eyes which have been enucleated because of absolute glaucoma, in search for its pathogenesis. Wide-angle glaucoma usually occurs in older people and it is generally recognized that many mild cases escape diagnosis. For these reasons we decided to examine our stock of "normal" eyes for subclinical glaucoma—the early lesions which form the obstruction to the aqueous outflow.

METHODS

Most of the eyes in the Eye-Bank library are from persons over 50 years of age, but eyes of all ages were examined. In addition to hematoxylin and eosin stain, periodic-acid fuchsin was used for collagen fibers and Verhoeff stain for elastic fibers. The phase-contrast microscope was found to be invaluable in the study of collagen fibers, because cases with marked pigmentation can be adequately studied only by this method. Much of the study required serial sections, which were cut both equatorially and sagittally, and were prepared for both quantitative and qualitative correlation of the pathologic process found. Peripheral sagittal sections, which are very similar in appearance to equatorial sections, were also quite valuable.

FINDINGS

A type of degeneration was found in many "normal" eyes which we have not seen reported in the literature. The *incidence* (tables 1 and 2) of this change is fairly high after the age of 40 years. We examined 2,792 eyes, using from three to 20 slides from each eye, and found varying degrees of degeneration in 10.4 percent. It is rarely present in younger adults, and has not yet been found in babies' eyes. More detailed study, with a great number of sections, was made of positive cases. Since the etiology of the degenerative process is as yet unknown, we have called it primary degeneration.

The location of the degeneration is in the drainage area. It is most often found in the external portion of the trabecula (figs.

* Under the auspices of The Eye-Bank for Sight Restoration, aided by U. S. Army Contract DA 49 007 MD 455 and by Grant B 153 (C2) from the United States Department of Health, Education, and Welfare and by The Josiah Macy, Jr., Foundation.

TABLE 1

INCIDENCE OF DEGENERATION IN VARIOUS AGE GROUPS

Age Group (years)	Eyes Examined	Eyes Showing Degeneration	Percent
Newborn—20	377	None	—
21–30	99	3	3.0
31–40	181	8	4.4
41–50	330	40	12.1
51–60	571	73	12.8
61–70	540	70	12.9
71–80	382	47	12.3
81–90	90	13	14.4
91–100	13	1	7.2
Unknown	209	35	—

2, 3, and 4), where the fibers are usually thinner and more compactly arranged. We assume that this is the site of the primary lesion. It spreads along collagen fibers. It may spread either externally or internally to the wall of Schlemm's canal, to the collector channels (fig. 5), and even to the intrascleral plexus. The walls of these channels and other adjacent tissue may be destroyed in the process.

The nature of the degeneration is not entirely clear, but it attacks the ground substance of the collagen first. The earliest change is a fragmentation of the intercellular substances (fig. 15) in the form of a breakdown of the collagen into granules, followed by their disappearance, leaving the endothelium, connective-tissue cells and nuclei apparently intact (fig. 3).

Elastic fibers are more resistant than collagen but they also degenerate eventually. The "glass membrane" of the trabecula is not consistently demonstrated by stain, so our studies of this membrane have been inconclusive.

TABLE 2

INCIDENCE OF DEGENERATION ACCORDING TO SEX

Sex	Eyes Examined	Eyes Showing Degeneration	Percent
Male	1464	157	10.7
Female	1060	121	11.4
Unknown	268	12	—

Changes in the endothelium, however, may play a very important role. Endothelium is very delicate and prone to injury, and endothelial cells tend to degenerate and decrease in old age. For these reasons we have confined our remarks about endothelial findings to the one change that was demonstrable beyond doubt, namely proliferation (figs. 6 and 8).

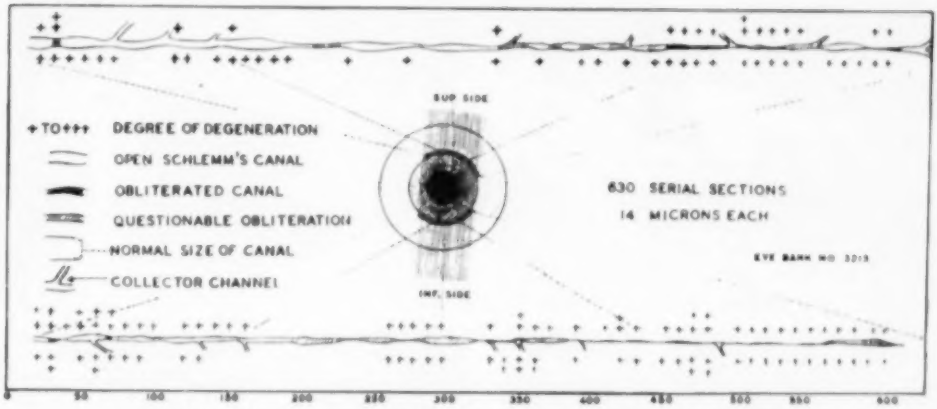
In the trabecular region, after the degeneration of the collagen and elastic fibers, the endothelial cells proliferate to form an edematous, spongy mass (figs. 9 and 10) or a compact, laminated membrane (figs. 12 and 13), which appears to be due to dehydration. The membrane is similar in appearance to a bundle of fibrous cells, except that the degenerated tissue does not take any stain. The endothelial cells may proliferate and extend into Schlemm's canal, into collector channels, and even into the intrascleral plexus (fig. 14). Occasionally there is a small area of round-cell infiltration either in the perivascular region, in the walls of Schlemm's canal, or in the walls of a collector channel, a change which we think is secondary.

INTERPRETATION

Decreased facility or increased resistance to the outflow of aqueous results from these pathologic processes. This result may be the product of one or several processes:

I. CHANGES AT THE INNER WALL OF SCHLEMM'S CANAL AND THE TRABECULA (figs. 6 and 10)

The loss of collagen causes the collapse of the trabecular meshwork and obliteration of the trabecular spaces. There is a strong tendency for adhesions to form between the degenerated trabecular fibers. As a result, the sievelike structure of the inner wall of Schlemm's canal is destroyed. The amount of decrease in the facility of the outflow is de-



Graph 1 (Teng, Paton, and Katzin). Results of serial section study in *Case 1*.

pendent upon the size of the area affected by the degeneration.

II. Adhesions between the walls of Schlemm's canal (figs. 7, 8, 9, 11, and 12)

The degenerative lesion on the inner wall of Schlemm's canal exhibits a tendency to adhere to the external wall. From this area of adhesion the degeneration may spread into the sclera and then further along the collagen fibers (fig. 9). These adhesions narrow down the lumen of Schlemm's canal. This is significant because a relatively few adhesions can eventually obliterate a great part of Schlemm's canal.

In the three cases presented, this mechanism was observed to be an important factor in causing the obstruction of Schlemm's canal.

There is considerable variation in the degree of obstruction; in severe cases all of Schlemm's canal may be obliterated.

III. Obstruction of the collector channels (figs. 11, 13, and 14)

This is a dangerous form of obstruction to the outflow of aqueous because there are only 20 to 30 of this kind of exit channel from Schlemm's canal in each eye.

The obstruction of the channel is found to be accomplished in the following ways:

1. Degeneration resulting in proliferation and swelling of the endothelium of the collector channels.

2. After the degeneration of the collagen around the channels, the connective tissue cells become distorted, due either to edema or to dehydration. Thus the lumen is obliterated.

3. The degeneration may destroy the channel completely, involving the whole region.

When the degenerative process involves the intrascleral plexus, the result is not so serious because of the existence of free anastomosis in the plexus.

Report of three cases of wide-angle glaucoma

Case 1

(EB 3212 and 3213—figs. 15, 16, 17, 18, 19, and 20)

The patient was a man, aged 57 years, who died of cardiovascular disease. There was a history of glaucoma, but no details were available.

Serial section study (graph 1)

A. 3213 (O.D.). The cornea and other parts of the eye were essentially normal. There was primary degeneration of the trabecula. The degeneration appeared mostly

in the external layers of the trabecula or in the inner wall of Schlemm's canal, but it was very widespread and there were many adhesions between the external wall of Schlemm's canal and the lumen was very much narrowed. Many of the collector channels were obliterated or destroyed due to adhesions and proliferation of endothelium. It was estimated that only about 10 to 20 percent of the facility of aqueous outflow remained. We judged that there must have been an elevation of tension.

The optic nerve showed no excavation but there was poor staining in areas of the section and some degeneration around the central blood vessels.

Although the history was not complete, the pathologic picture was obviously one of wide-angle glaucoma. The evidence of this was mainly in the corneoscleral wall of the anterior chamber angle—there was very little change at the disc. Judging from the quantity of pathologic change, there was enough to cause a rise of ocular tension.

The nature of the pathologic change at the chamber angle was very much the same as we found in the "normal" or subclinical cases. This change we judged to be included in the pathogenesis of wide-angle glaucoma.

B. 3212 (O.S.). The cornea and other parts of the eye were essentially normal, except that the chamber angle was collapsed after removal of the corneal disc for graft. There were no real peripheral synechias. Otherwise the pathologic changes were very similar to those in the right eye.

CASE 2

(EB 105 and 106—figs. 21, 22, 23, 24, 25, and 26)

The patient was a woman, aged 77 years. Cause of death was given as fracture of the femur. She had a known history of glaucoma and a trephining operation had been done but there were no further details available.

Serial section study (graph 2)

A. EB 106 (O.D.). This eye had a good functional cystoid bleb over the patent trephine hole. There was no pigmentation on the endothelial side at the lip of the trephine hole which means that there were no peripheral synechias before the trephination, and the iridectomy was well done. The partial peripheral synechias were thought to have developed postoperatively. There was extensive primary degeneration around Schlemm's canal and the collector channels and extensive obliteration due to adhesions and proliferation of endothelium.

From the serial section reconstruction, Schlemm's canal was found to be obstructed in a major portion and the rest of the lumen was much narrowed down due to adhesions between the walls. The trabecula showed extensive and widespread degeneration.

From the extent of obstruction and degenerative change, we believe this to have been a case of wide-angle glaucoma. The peripheral synechias must have been secondary, because the inner portion of the

Fig. 1 (EB 123) Degeneration often occurs in the trabecula near Schlemm's canal with deposition of pigment, while the endothelial cells seem to remain intact (hematoxylin-eosin stain).

Fig. 2 (EB 2310) Loss of collagen in the degenerated trabecular fibers (Van Gieson stain).

Fig. 3 (EB 2310) Loss of elastic fibers in the degenerated area. Elastic fibers are usually more resistant than collagen (Verhoeff stain).

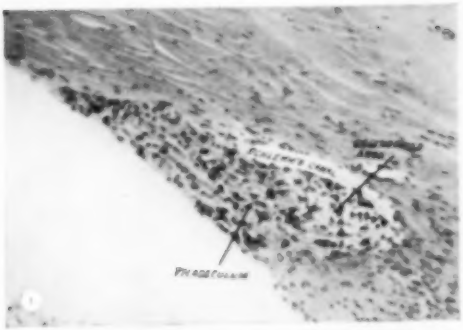
Fig. 4 (EB 2310) Glass membrane changes are not satisfactorily demonstrated, but this figure shows loss of substance in the degenerated trabecula (periodic acid-fuchsin stain).

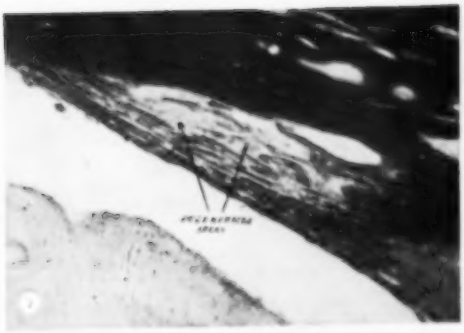
Fig. 5 (EB 2338) Degeneration shows as faded area around collector channels. Connective tissue cells remain intact, but there is a disappearance of connective tissue matrix (hematoxylin-eosin stain).

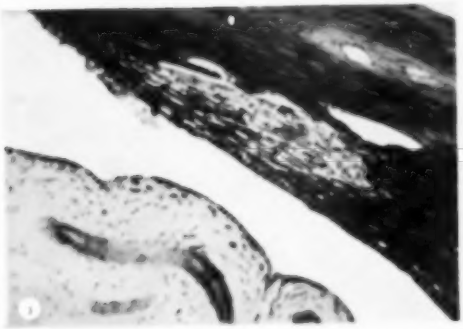
Fig. 6 (EB 2297) Degenerated area appears slightly spongy; some proliferation of endothelial cells and obliteration of trabecular spaces (hematoxylin-eosin stain; equatorial section).

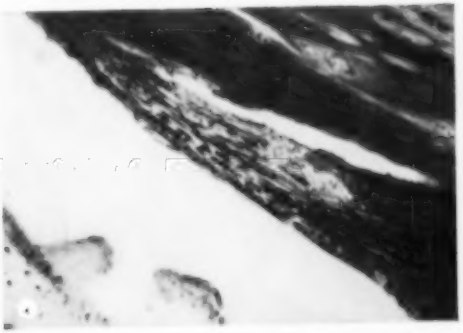
Fig. 7 (EB 2243) Mild degeneration, spongy appearance, and adhesions between the walls of Schlemm's canal in two areas (Verhoeff stain; equatorial section).

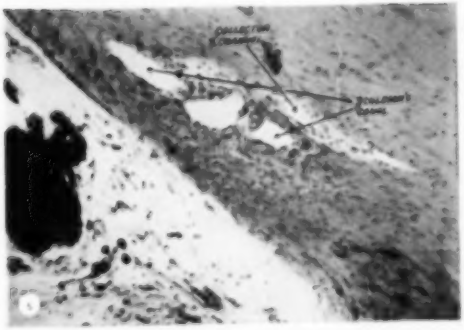
Fig. 8 (EB 2338) Extensive adhesion between the walls of Schlemm's canal, with proliferation of endothelium (hematoxylin-eosin stain; equatorial section).

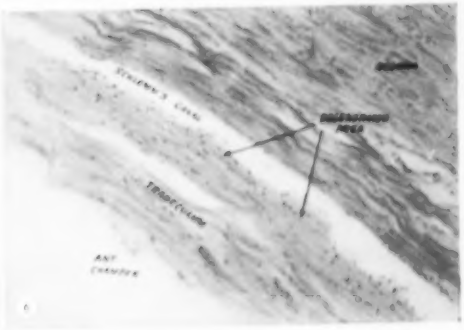








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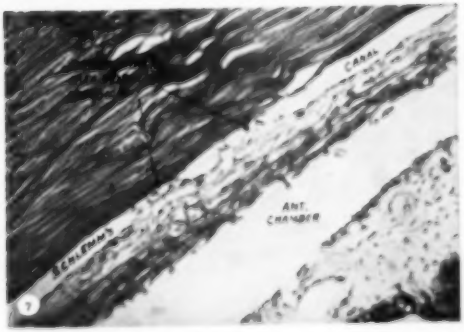
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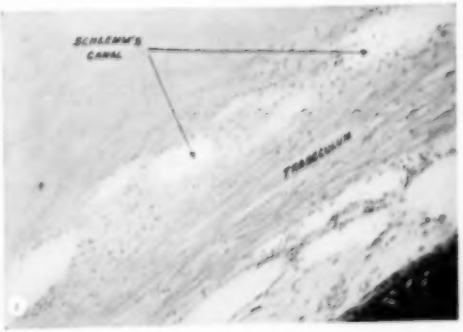
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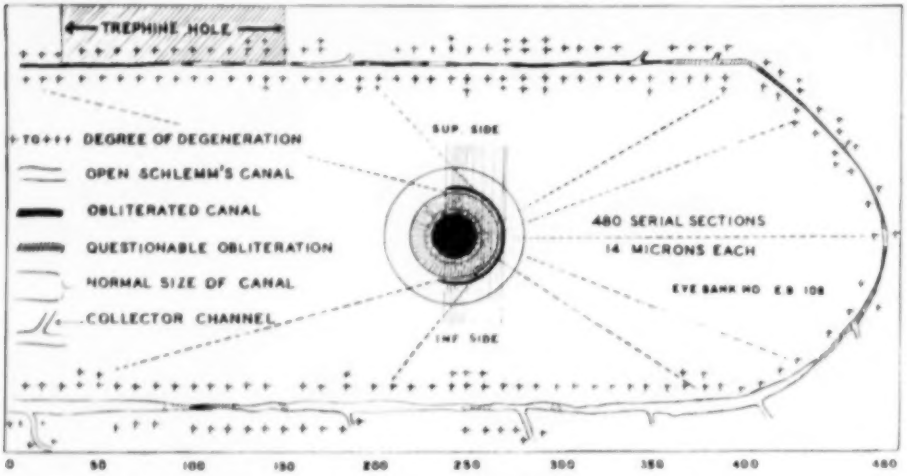


Graph 2 (Teng, Paton, and Katzin). Results of serial section study in *Case 2*.

trabecula showed no sign of compression and the trabecular spaces were all in good condition. There were adhesions, but no sign of compression from intraocular pressure. We assume this was due to the success of the trephining operation. There was no cupping of the optic disc, but there was some superficial degeneration of the optic-nerve head.

B. EB 106 (O.S.). The left eye had a similar, but milder, pathologic picture, without any peripheral synechias. This helped confirm our theory that the peripheral synechias in the right eye were secondary to surgery.

CASE 3*

(EB 854 and 855—figs. 27, 28, 29, 30, 31, and 32)

Clinical history. The patient was a man, aged 56 years, who died of a cerebrovascular accident. Eye tension was reported between 25 to 30 mm. Hg. The visual fields had large Bjerrum scotomas which reached across the maculas.

Gonioscopic study. O.D.: The angle was closed off all around. In the lower part of the

* This case was obtained through the kind cooperation of Dr. Francis H. Adler and Dr. Harold G. Scheie.

Fig. 9 (EB 2338) Same as Figure 8. Shows degeneration spreading to the sclera along the collagen fibers (Van Gieson stain; equatorial section).

Fig. 10 (EB 725) Shows degeneration of the trabecula adjacent to Schlemm's canal, and obliteration of the trabecular spaces (hematoxylin-eosin stain).

Fig. 11 (EB 758) Schlemm's canal is almost completely obliterated and the collector channel is about half occluded (hematoxylin-eosin stain).

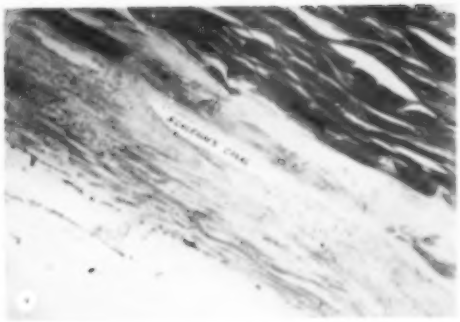
Fig. 12 (EB 2890) Degenerated tissue in compact form obliterates all but a small remnant of Schlemm's canal (periodic acid-fuchsin stain).

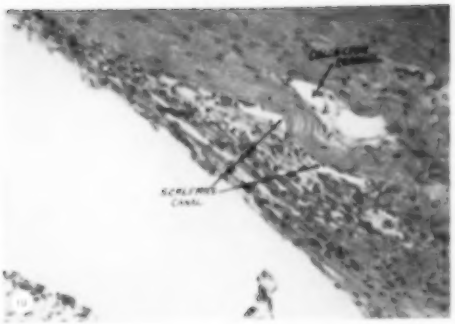
Fig. 13 (EB 2338) Compact degenerated tissue obliterates the collector channels. Here Schlemm's canal is open (hematoxylin-eosin stain).

Fig. 14 (EB 2318) Extensive degeneration around Schlemm's canal and collector channels (Verhoeff stain).

Fig. 15 (EB 3213) Early degeneration of collagen shows as granular change in the fibers of the trabecula (Van Gieson stain).

Fig. 16 (EB 3212) Obliteration of Schlemm's canal due to degeneration, adhesion of the walls, and proliferation of endothelium (Van Gieson stain).

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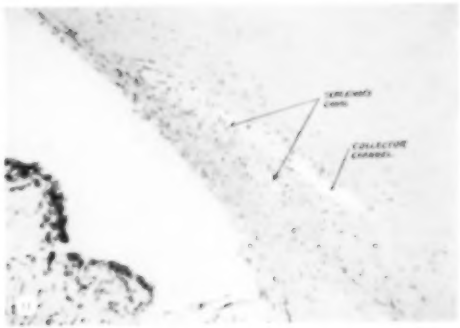
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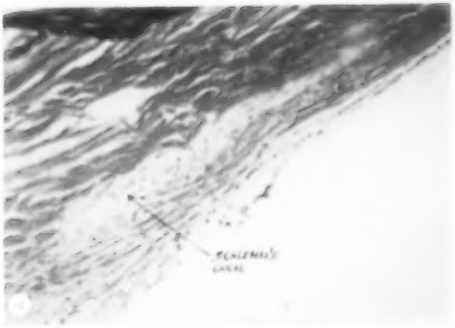
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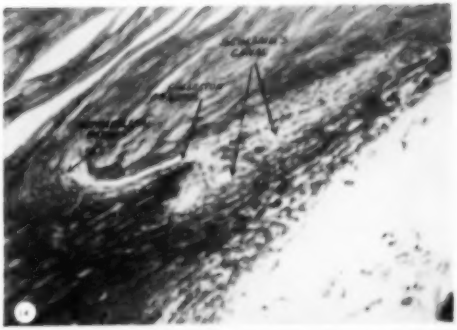
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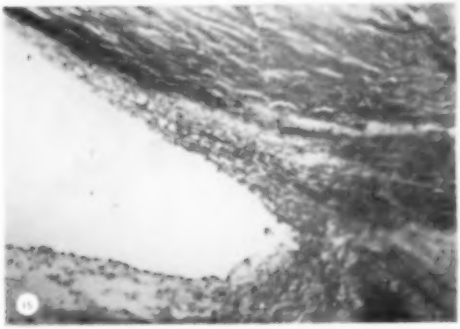
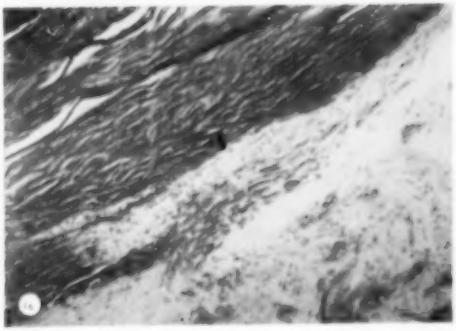
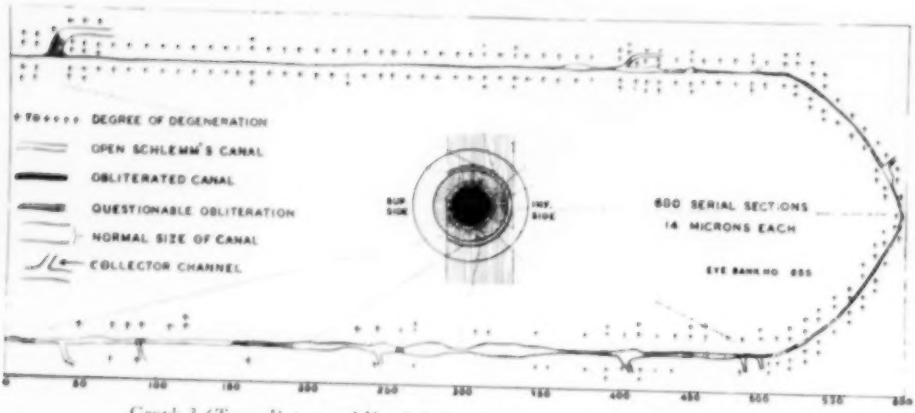






Graph 3 (Teng, Paton, and Katzin). Results of serial section study in *Case 3*.

angle Schwalbe's line could be seen but nothing further was visible.

O.S.: The trabecula could be seen all the way around. Many small peripheral synechias were present.

The discs were pale and cupped, especially on the right side.

The last visit was two and one-half months before death.

O.D.: Blind, tension 25 mm. Hg, pupil miotic.

O.S.: Vision *6/60*, tension *30* mm. Hg, pupil miotic.

Serial section study (graph 3)

The pathologic findings in both eyes were about the same:

Chamber angle. Most of the area around Schlemm's canal showed typical primary degeneration with multiple adhesions and mild proliferation of endothelium. From the reconstructed sections it was estimated that about 80 percent of Schlemm's canal was obstructed and many of the collector channels were obliterated by the same pathologic process.

Optic discs. In both eyes there was sharp-edged, fairly deep cupping of the optic discs. Their surfaces were covered by glial tissue. There was degeneration of nerve-fiber tissue, collagen, and some elastic fibers. (This type of degeneration of the optic nervehead will be covered by a separate study.)

The degeneration of nerve-fiber tissue occurred mostly inside the lamina cribrosa and it was replaced by glial tissue. The de-

Fig. 17 (EB 3213) Similar degenerative changes around Schlemm's canal extending into the collector channel (Van Gieson stain).

Fig. 18 (EB 3212) Similar changes to those in the preceding picture (Van Gieson stain; equatorial section).

Fig. 19 (EB 3212) Mild degeneration of inner wall of Schlemm's canal, with adhesion and obliteration of the lumen (Verhoeff stain; equatorial section).

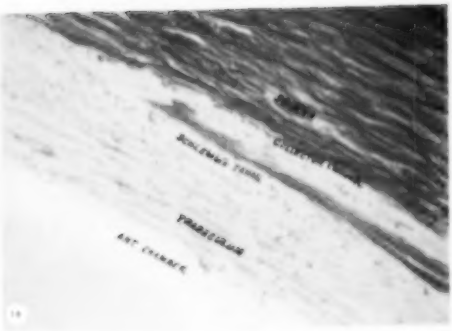
Fig. 20 (EB 3213) Optic disc. Slight degeneration around blood vessels (hematoxylin-eosin stain).

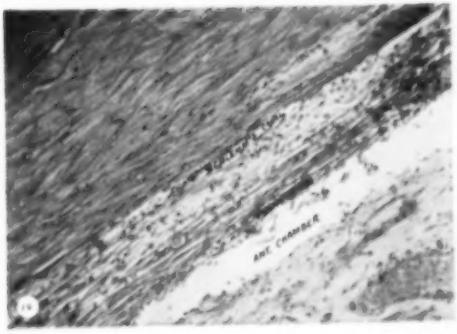
Fig. 21 (EB 106) A functional trephine bleb with peripheral anterior synechias near the wound (Van Gieson stain).

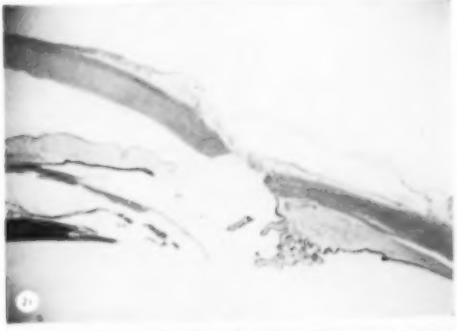
Fig. 22 (EB 106) Degeneration around Schlemm's canal and collector channels with proliferation of endothelium and obliteration. This figure shows marked pathologic changes (Van Gieson stain).

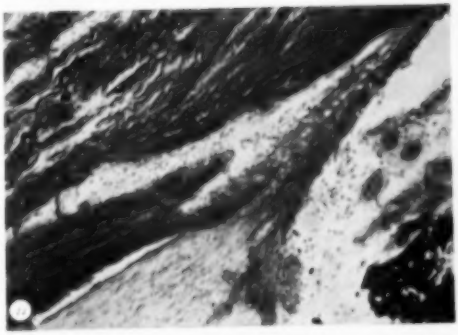
Fig. 23 (EB 106) Degeneration around Schlemm's canal and collector channels, with proliferation of endothelium and obliteration (Van Gieson stain; equatorial section).

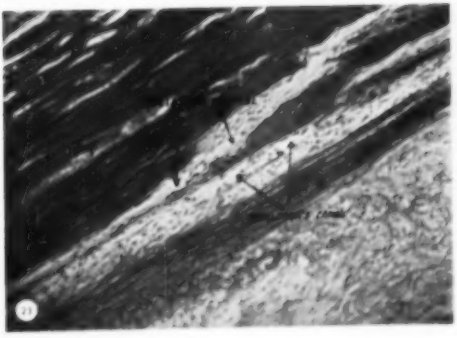
Fig. 24 (EB 106) Similar to Figure 23 but with less proliferation of endothelium. (When glaucoma is of long standing or uncontrolled, the degenerated tissue becomes more compressed.) (Van Gieson stain.)

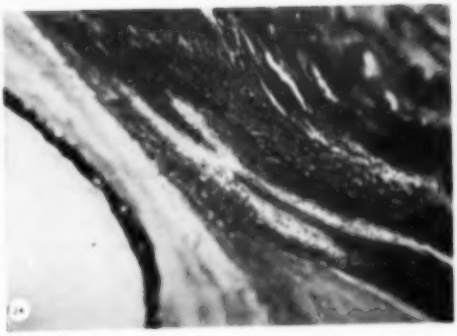












gree of cupping is in proportion to the degree of collagen degeneration in the lamina cribrosa. There was no change noticed in the blood vessels.

This was a case of wide-angle glaucoma with mild increase in ocular tension, but with degeneration of the optic nerve and deep excavation.

Comment

The theory of through-and-through circulation of the aqueous was first offered by Leber and later confirmed by Ascher's[1] work on aqueous veins. This work also indicated that the anterior chamber angle is the main route for aqueous drainage.

Following the lead of Kronfeld,[2] the current method of tonography was developed by Moses and Bruno,[3] and Grant.[4] These investigators noticed the low co-efficient of outflow in chronic glaucomatous eyes. Using Friedenwald's[5] data for pressure and volume relationship in the analysis of the tonographic data, Grant concluded that the cause of wide-angle glaucoma is decreased facility or increased resistance to the aqueous outflow rather than hyperformation of aqueous humor.

Barkan,[6] in correlating his clinical observations, predicted that the impediment to outflow would be located within the trabecula or the angle wall. Ascher theorized that the impediment was in the collector channels centripetal to Schlemm's canal. Ashton's observations with Neoprene injection tend to support this suggestion. We fully realize that the gonioscope cannot easily detect primary degeneration because the lesion is usually in the external group of the trabecular fibers.

Kronfeld, McGarry, and Smith[26] observed a few cases of advanced wide-angle glaucoma in which the trabecula was less transparent than normal. Barkan found that in 90 percent of his wide-angle glaucoma cases, a gonioscopic examination showed reduced penetration of light, a manifestation of more compact and impermeable structure. Again he noticed that tissues in cases of wide-angle glaucoma are prone to react abnormally to surgery in that they have an increased tendency to formation of adhesions and deposition of pigment. This fact plus the higher incidence of pigment disturbance led Barkan to suggest that the tissues of the eyes are diseased in wide-angle glaucoma in comparison to the initially healthy tissue in narrow-angle glaucoma, where the same tendencies are not exhibited.

The blood-filling phenomenon of the canal of Schlemm has been studied very extensively by Kronfeld and his associates.[26] Two methods were used to produce this phenomenon in normal eyes: (1) Withdrawal of aqueous by needle puncture and (2) compression of the eyeball by means of Kuk'un's ophthalmodynamometer. They noticed that the presence of blood in the canal of Schlemm could be established in every one of those normal eyes except those few in which

Fig. 25 (EB 106) Schlemm's canal and the collector channel seen on the left side are normal. On the right side Schlemm's canal is completely obliterated (hematoxylin-eosin; equatorial section).

Fig. 26 (EB 106) Optic disc. No cupping (periodic acid-fuchsin stain).

Fig. 27 (EB 854) Degeneration of the trabecula plus adhesions cause complete obliteration of Schlemm's canal. Pigment must have been deposited before obliteration (hematoxylin-eosin stain).

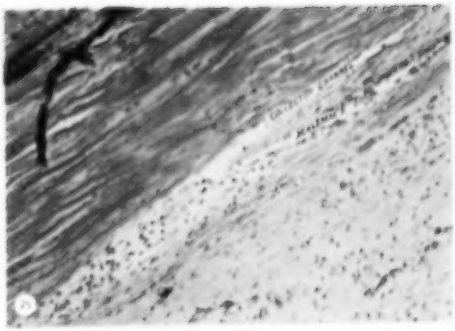
Fig. 28 (EB 855) Degeneration around Schlemm's canal and collector channels (Van Gieson stain).

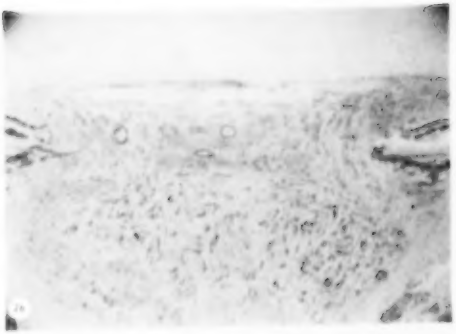
Fig. 29 (EB 855) Degeneration, adhesions, and obliteration of Schlemm's canal (hematoxylin-eosin stain; equatorial section).

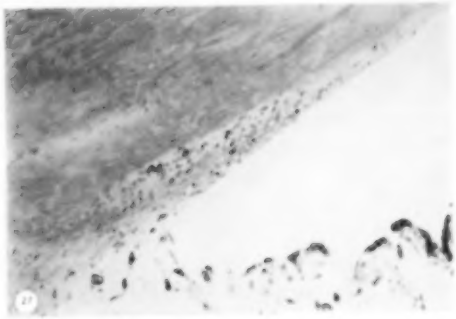
Fig. 30 (EB 855) Sharp cupping of the optic-nerve disc which was covered with glial tissue. There is no sclerotic change in the blood vessels (hematoxylin-eosin stain).

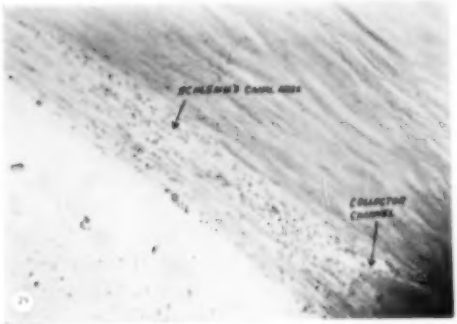
Fig. 31 (EB 855) Different area shows degeneration of collagen at the lamina cribrosa and deep cupping formation (Van Gieson stain).

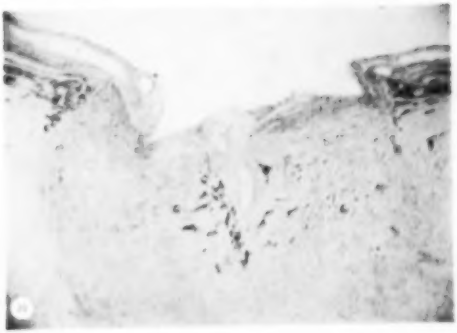
Fig. 32 (EB 855) Similar to above picture. Some areas show degeneration of elastic fibers (Verhoeff stain).

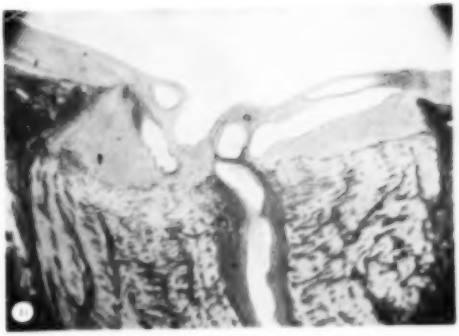


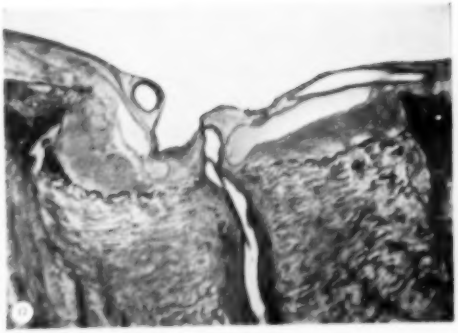





SCHLEMM'S CANAL AREA
COLLECTOR CHANNEL







the visibility was poor because of large amounts of fibrin in the secondary aqueous. In wide-angle glaucomatous eyes they noted different phenomena: (1) Completely non-filling, (2) a grossly segmented band, (3) narrowing of the band, and (4) opaque trabecula with some filling of the canal.

Barkan also observed that the Schlemm's canal zone of the trabecula and the blood-filled Schlemm's canal were abnormally narrow in wide-angle glaucoma.

Ascher reported that there are fewer cases with aqueous veins in wide-angle glaucoma and that the flow decreases and becomes slower.

Goldmann[7] also found that the outflow of aqueous through the aqueous veins was markedly diminished in chronic simple glaucoma and interpreted this decrease as due to increased resistance to the outflow through the trabecula.

All of these observations could be explained by obstruction due to primary degeneration in the trabecula, Schlemm's canal, and the collector channels, such as we have demonstrated.

Kronfeld's blood-filling phenomenon may be a good test for the patency of the collector channels and Schlemm's canal. It may even help break fresh, weak adhesions. But there are limitations for this test, as in a case where the passage is smaller than the diameter of a red blood cell.

As to the nature of the degeneration, it is not congenital because it is not found in babies' eyes. There is no inflammatory change. Occasionally there is some white blood cell infiltration, but this is most probably secondary.

The possibility that these are postmortem changes has been ruled out by comparison with the most sensitive portion of the eye, the retina. The degeneration we have described is localized, while postmortem changes are more diffuse and general. Also, primary degeneration of the chamber angle includes the reactive changes of living tissue, such as endothelial proliferation and the formation of adhesions.

The main feature of primary degeneration is that the early changes appear in the intercellular substance of the trabecula in the form of fragmentation of the collagen into granules followed by their disappearance. This is followed by the disappearance of elastic fibers. It seems that the cell bodies and nuclei remain intact. The endothelial cells often show proliferation. The cell body may become edematous or may be found in a dehydrated, compact form. We also noted the disappearance of the glass membrane, but we have not been able to demonstrate the degenerative steps leading to it. In the endothelium we can only demonstrate with certainty the proliferative reaction to degenerative changes.

The cause of the degeneration is unknown but from the nature of the changes, we think it may be due to one or more proteolytic enzymes or simply a solublization process. Proteolytic enzymes have been demonstrated in the aqueous, but as yet there has been no detailed investigation of this subject.

Summary

A type of degeneration was found in the wall of the anterior chamber angle, the cause of which is unknown.

It probably begins most often in the external trabecular region and spreads along these fibers internally or externally to Schlemm's canal, to the collector channels and sometimes to the intrascleral plexus.

The nature of the degeneration is not entirely clear, but the degeneration of collagen and elastic fibers was demonstrated. Due to these degenerative processes and the subsequent formation of adhesions and proliferation of endothelium, the drainage channels were obliterated.

Three early cases of wide-angle glaucoma were reported and found to exhibit the same type of degeneration in more extensive and advanced forms.

Our studies suggest that wide-angle glaucoma is a degenerative disease involving the wall of the anterior chamber angle.

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REFERENCES

1. Ascher, K. W.: Aqueous veins: Their status eleven years after their detection. Arch. Ophth., **49**:438, 1953.
2. Kronfeld, P. C.: Tonography. Arch. Ophth., **48**:393, 1952.
2b. Kronfeld, P. C., McGarry, I., and Smith, M. E.: Gonioscopic studies on the canal of Schlemm. Am. J. Ophth., **25**:1163, 1942.
2c. Kronfeld, P. C.: Further gonioscopic studies on the canal of Schlemm. Arch. Ophth., **41**:393, 1949.
3. Moses, R. A., and Bruno, M.: Ratio of outflow of fluid from the eye under increased pressure. Am. J. Ophth., **33**:389, 1950.
4a. Grant, W. M.: Tonographic method for measuring the facility and rate of aqueous flow in human eyes. Arch. Ophth., **44**:204, 1950.
4b. ———.: Clinical measurements of aqueous outflow, with discussion by Friedenwald. Arch. Ophth., **46**:113, 1951.
4c. ———.: Clinical tonography. Tr. Am. Acad. Ophth., **56**:774, 1951.
5. Friedenwald, J. S.: Abstract of discussion of Grant's paper, 4b.
6. Barkan, O.: Primary glaucoma: Pathogenesis and classification. Am. J. Ophth., **37**:724, 1954.
7. Goldmann, H.: Pressure rapidity of outflow and resistance to the circulation of the aqueous humor in man. Documenta Ophth., **5-6**:278, 1951.
8. Adler, F. H.: Physiology of the Eye: Clinical Application. St. Louis, Mosby, 1953. p. 93.

THE HISTOPATHOLOGY OF THE ACUTE AND CHRONIC OCULAR HYPERSENSITIVE REACTIONS IN THE EXPERIMENTAL RABBIT*

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In another publication[1] one of us (A. C. W.) has pointed out that endogenous uveitis, from clinical and pathogenetic viewpoints, may be separated into two entities. These have been termed "granulomatous" and "nongranulomatous."

Granulomatous uveitis has a characteristic symptomatology and is believed to be caused by a direct infection of the uvea with various nonpyogenic infectious agents.

Nongranulomatous uveitis also has a characteristic clinical picture and it is assumed to be a sterile reaction and result from an acute tissue insult. This insult is usually allergic but may be toxic or physical.

We have also expressed the view that in the active stages the histopathology of granulomatous and nongranulomatous uveitis is usually quite different. The characteristic change in granulomatous uveitis is a tuberculoid reaction, and in nongranulomatous uveitis is nonspecific inflammation. In the active stages of both diseases, the histologic differentiation can usually be readily made. As both conditions progress and become burned out, they tend to lose their characteristic histologic pictures, and finally differentiation may become difficult or even impossible.

This nomenclature has been criticized on the grounds that histologic terms are used to describe clinical and pathogenetic entities, and that frequently histologic differentiation of those entities may be impossible. This criticism is based on the arguments:

a. That in the atrophic or inactive stages the granulomatous uveitis loses its typical characteristic tuberculoid appearance and resembles the nonspecific inflammation and

* From the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital. This investigation was supported by a grant from the National Institute of Neurological Diseases and Blindness.

scarring seen in the end-stages of nongranulomatous disease.

b. Under certain conditions, which are not clearly understood, the histologic picture of an allergic reaction may closely resemble the tuberculoid reaction seen in classical granulomatous disease. This has been observed in clinical periarteritis nodosa[2, 3] and also in experimental periarteritis nodosa and serum sickness.[4, 5]

The validity of both of these arguments is at once admitted. The first argument, however, appears trivial. It is well known that the pictures of an active granulomatous tuberculoid change resulting from infection, and of acute nonspecific inflammation are quite different. It is of little moment that they may resemble each other in their inactive old age. The second point is much more important—Can allergic reactions in the eye produce the picture of granulomatous tuberculoid changes such as Rich found on the heart valves and in the spleen of rabbits with experimental periarteritis nodosa and serum sickness? If so, it may be necessary to revise our thinking of the meaning of the tuberculoid reaction in the eye.

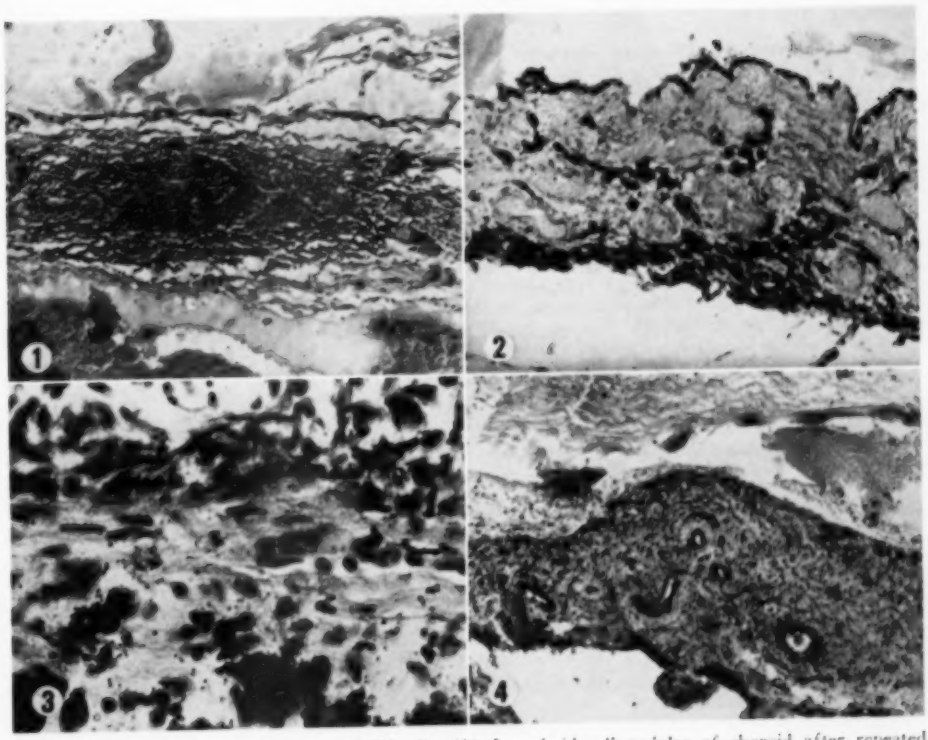
This question cannot be answered by the examination of human material. Eyes in the acute stage of nongranulomatous uveitis are never enucleated. There is no mortality in the disease and hence no material for examination. The only human eyes with allergic uveitis available are from patients with advanced rheumatoid arthritis who have gone blind from repeated attacks of nongranulomatous uveitis and whose phthisical eyes have been enucleated on account of pain. In the study of this material, all eyes with a history of rheumatic scleritis must be excluded, for it is well known that in such eyes there may be a granulomatous tuberculoid reaction around necrotic collagen.

A study of the limited material remaining shows that the usual histologic findings are nests and nodular accumulations of lymphocytes and plasma cells scattered throughout the choroid and pars plana of the ciliary body (fig. 1)—a change characteristic of prolonged chronic inflammation. One of these eyes which showed this change, also showed a change in the iris suggestive of a possible granulomatous reaction. This consisted of a sheet of fibroblasts with a number of epithelioid cells in the midstroma of the iris (fig. 2.—low power, fig. 3—high power). While this change is quite similar to that seen in old burned-out granulomatous uveitis, it is certainly not a characteristic tuberculoid reaction.

There has been amazingly little study of the histopathology of the experimental allergic reaction in the eye, and what there is appears somewhat contradictory. In 1943, Schlaegel and Davis[6] studied the histologic changes produced in the eyes of sensitized rabbits by single and multiple intravitreal injections of horse serum. The horse serum used for sensitization and ocular injection contained merthiolate as a preservative. They found the uveal tract infiltrated with lymphocytes, multinucleated giant cells, epithelioid cells, large mononuclears, and plasma cells. On the choroid there were occasionally sheets of these same wandering cells, forming a layer almost as thick as the normal retina. Their descriptions and illustrations suggest a granulomatous reaction.

The validity of these observations is possibly impaired by the extremely high mortality in their experimental animals–10 out of 22 dying during the period of sensitization. This raises the question that their rabbits may have had some unrelated infection, such as the common epizootic coccidial disease, the experimental ocular trauma facilitating the localization of endogenous infection in the eye.

In 1951, Biegel[7] studied the effect of cortisone on anaphylactic horse-serum uveitis. His untreated controls (sensitized rabbits subjected to one intravitreal injection of horse serum without a preservative) showed infiltration of the choroid and ciliary body with lymphocytes and plasma cells, together with occasional nests of cells beneath the



Figs. 1-4 (Woods, Friedenwald, and Wood). (1) Lymphoid cell nodules of choroid after repeated attacks of nongranulomatous uveitis (human). (2) Scarring of midzone of iris after repeated attacks of nongranulomatous uveitis (human, low power). (3) High-power view of (2). (4) Single acute allergic insult—24 hours—primary outpouring of leukocytes with sprinkling of lymphocytes and wandering cells. Fibrinous exudate in anterior chamber. Edema, cellular infiltration, and capillary dilatation of iris.

pigment epithelium, which suggested Dalen-Fuchs nodules. Dr. Biegel was kind enough to send us sections of these control eyes, and histologic examination showed these nests of cells were composed almost entirely of lymphocytes and plasma cells. Occasional epithelioid cells could be identified in them and also in the anterior choroid, but nowhere were any tuberculoid changes or epithelioid cell nodules found.

It is obvious that the question of the histology of the acute allergic ocular reaction cannot be determined by the study of human eyes and that the information thus far obtained from experimental studies is inadequate and conflicting. In the hope of clarifying the picture, we therefore undertook this present study of the histopathology of the experimental ocular allergic reaction. This study falls into three parts:

I. The histology of the acute allergic reaction produced by a single anterior injection of specific antigen.

II. The histology of a chronic and protracted allergic reaction produced by repeated anterior chamber injections.

III. The histology of an allergic reaction produced by single and multiple intravitreal injections.

Experimental technique

In the three experiments here reported, the test rabbits were sensitized to bacterial antigens and to horse serum in the following

manner:

A. *Bacterial antigen.* T-50 suspensions of a subgroup A Beta streptococcus and of B. abortus were used as antigens. The rabbits were given intravenous injections of 0.1, 0.2, and 0.3 cc. of these suspensions on the first three days of three consecutive weeks. After a rest period of several weeks they were tested for hypersensitivity by the intracutaneous injection of 0.1 cc. of a 1:10 dilution of the same specific bacterial antigen. If hypersensitivity had not developed they were given further "booster" injections. All animals were proven highly hypersensitive before the ocular injections were made.

B. *Horse serum.* A 1:10 dilution of sterile horse serum was used for sensitization.

In Experiments I and III, the rabbits were given intracutaneous injections of 0.1, 0.2, and 0.3 cc. on the first three days of three consecutive weeks. After a rest period they were then tested for sensitivity by the intracutaneous injection of 0.1 cc. of the horse serum antigen. Only rabbits proven hypersensitive were used as test animals.

In Experiment II, the animals were given the intravenous injections as above, and after a short rest period were then given a further injection of 15 cc. of the undiluted horse serum. As a result of this procedure a high percentage of the animals died of anaphylactic shock. Of the survivors two rabbits became completely desensitized and were thereafter used as additional controls. The remaining survivors, which showed a persisting sensitivity with circulating antigen demonstrable in the blood, were used as the test animals.

C. *Anterior chamber injections.* The eye was anesthetized and then proptosed. Two-tenths cc. of the specific antigen was taken up in a tuberculin syringe. After puncture of the anterior chamber, 0.2 cc. of the aqueous was withdrawn in the syringe and 0.2 cc. of the resulting mixture was reinjected. This was repeated several times and 0.2 cc. of the final mixture of antigen and aqueous injected in the anterior chamber.

D. *Intravitreal injections.* The eye was prepared as above described. Two-tenths cc. of the antigen or material to be injected was taken up in a tuberculin syringe with a 28-gauge needle. A sharp stab puncture was made in the region of the equator between the vortex veins and after the injection the needle was immediately withdrawn. There was a slight transient elevation of the ocular tension, and a small amount of the injected material escaped through the puncture hole. There were no immediate untoward reactions.

Results

Experiment I

Single, acute, allergic insult from anterior chamber injections.

Four rabbits sensitized to streptococcus antigen, four sensitized to Brucella abortus antigen, and four sensitized to horse serum were used in this experiment. One rabbit from each of the three groups was killed 24 hours after the anterior chamber injection. The other three rabbits were killed respectively on the fourth, eighth, and 10th days.

Controls. A series of normal rabbits were given anterior chamber injections of the bacterial and horse serum antigens exactly similar to those given the sensitized animals. These rabbits were killed at the end of 24 hours, and on the fourth, eighth, and 10th days.

Clinical reaction in test animals. There was no marked difference in the clinical or histologic pictures produced by the bacterial and protein antigens. As would be expected with a less soluble and more slowly absorbed antigen, the inflammation produced by the bacterial antigens was somewhat delayed and more prolonged than that produced by the more readily absorbed horse serum.

All rabbits showed a typical acute nongranulomatous reaction, differing only in severity. The clinical course of this acute reaction was as follows:

Twenty-four hours after injection of the bacterial antigens, the eyes showed a violent pericorneal congestion, an acutely inflamed iris, a contracted pupil, and some fibrin in the anterior chamber. They were graded as from "1" to "4" in severity on the same scale used in previous experiments.[8] By the fourth day the reaction had largely subsided, with only a small amount of fibrin remaining in the anterior chamber. By the sixth day there was only a trace of residual inflammation remaining, and by the 10th day the eyes appeared entirely inactive.

Two of the horse serum sensitive rabbits were given 0.1 cc. of undiluted horse serum and the other two were given 0.1 cc. of a 1:10 dilution. The initial reaction of the rabbits receiving the undiluted serum was somewhat more intense than that shown by the animals receiving the diluted serum. Otherwise the reactions were identical. By

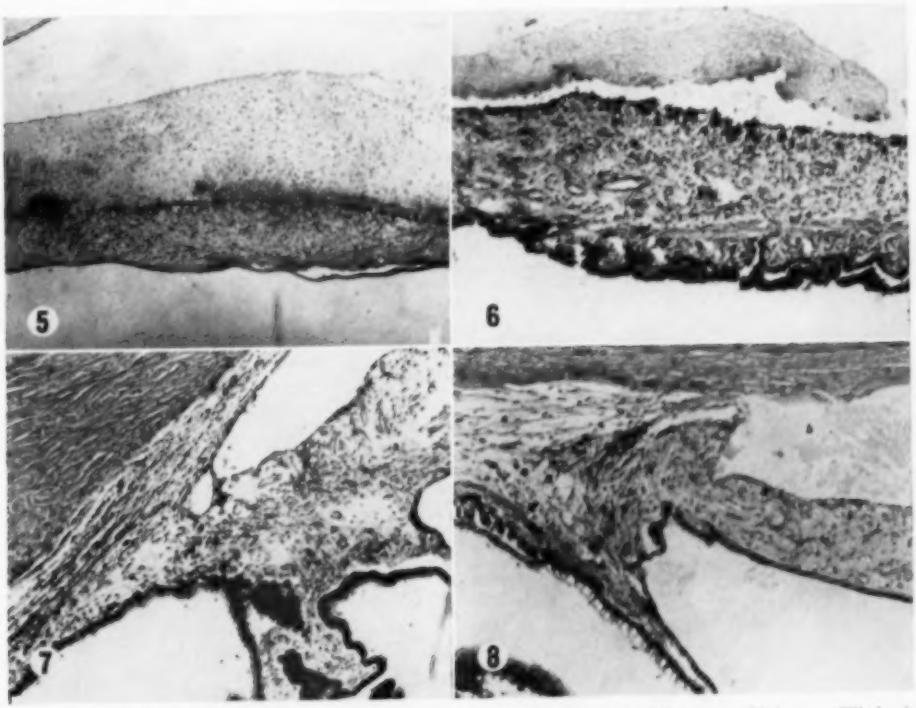
the end of the third day the inflammatory reaction in all four of the rabbits had largely subsided and was completely gone at the end of the eighth day.

Clinical reaction in controls. All control rabbits showed minimal reactions to the anterior chamber injections, varying from a mere trace of inflammation to a maximum of "0.5" at the end of 24 hours. By the second day the eyes had completely recovered and thereafter remained free of inflammation.

Histologic changes in test animals. Immediately after death, the injected eyes were removed, fixed in Zenker's solution, embedded in paraffin, sectioned, and stained with eosin and hematoxylin.

The histologic picture in all the eyes, whether sensitized to bacterial antigens or to horse serum, showed the same general pattern of inflammation.

The immediate reaction at the end of 24 hours was an outpouring of polymorphonuclear leukocytes, among which were a sprinkling of lymphocytes and large mononuclear macrophages. Heavy collections of these cells were found at the limbus, and scattered over the iris surface (fig. 4). There was a fibrinoserous exudation in the anterior chamber and enmeshed in this were many cells, chiefly leukocytes (fig. 5). There was a moderate cellular infiltration



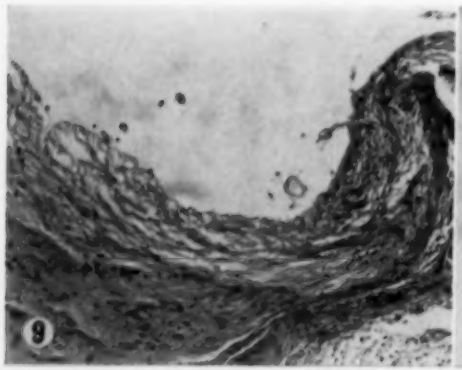
Figs. 5-8 (Woods, Friedenwald, and Wood). (5) Single acute allergic insult—24 hours. Fibrin in anterior chamber and collections of polymorphonuclear leukocytes on anterior surface of iris. (6) Single acute allergic insult—fourth day. Residual edema and capillary dilatation of iris. Absorbing exudate in anterior chamber. Leukocytes now almost entirely replaced by lymphocytes and plasma cells. (7) Single acute allergic insult—eighth day. All anterior chamber exudate absorbed. Subsiding edema and capillary dilatation of iris. Persisting lymphocytes, plasma and wandering cells at limbus. (8) Single acute allergic insult—10th day. Essentially normal anterior ocular segment.

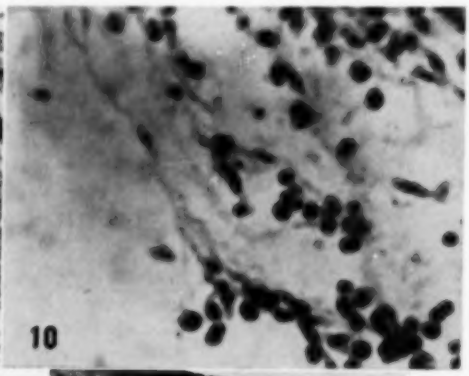
of the iris and ciliary body, and marked edema and capillary dilatation of the iris.

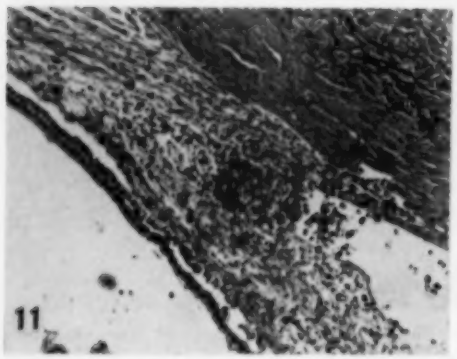
At the end of 96 hours the picture had radically changed. The leukocytes were largely replaced by lymphocytes, although there were still some polymorphonuclear cells present. A number of plasma cells could now be identified. The fibrinous exudate in the anterior chamber was largely absorbed and the enmeshed cells were now chiefly lymphocytes (fig. 6). The cellular infiltration of the iris was still marked and the edema and capillary dilatation of the iris still persisted. There was moderate cellular infiltration and slight edema in the ciliary body, and a minimal inflammatory reaction in the anterior choroid.

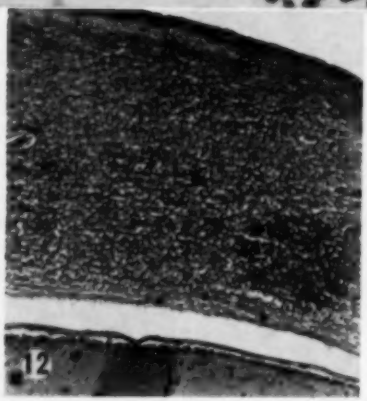
At the end of the eighth day the reaction had almost completely subsided. All serum, fibrin, and cells, except for a few persisting wandering cells at the limbus, were gone from the anterior chamber. The edema and capillary dilatation of the iris had disappeared and only a few lymphocytes and plasma cells remained in the iris stroma (fig. 7).

At the end of the 10th day the anterior ocular segment appeared practically normal (fig. 8). In the physiologic cup of the optic nerve there were still a few inflammatory









Figs. 9-12 (Woods, Friedenwald, and Wood). (9) Single acute allergic insult—10th day. Physiologic cup with a few remaining inflammatory cells (low power). (10) Ibid. Lymphocytes and plasma cells in physiologic cup (high power). (11) Single allergic insult—control—maximum reaction at 24 hours. (12) Protracted allergic insult from repeated anterior chamber injections. Vascularization, edema, and cellular infiltration of cornea.

cells (fig. 9), apparently striving to escape from the eye by this route. On high-power examination these cells were lymphocytes and plasma cells with an occasional large macrophage (fig. 10).

Histologic changes in controls. The control eyes, injected with horse serum and bacterial antigens, respectively, and enucleated at the end of 24 hours, showed a minimal inflammatory reaction—the maximum being a small localized nest of lymphocytes and leukocytes in the chamber angle, and a few wandering cells in the iris (fig. 11). The control eyes enucleated on the fourth, eighth, and 10th days were all normal.

EXPERIMENT II

Protracted allergic reaction produced by repeated anterior ocular injections.

Six rabbits sensitized to a streptococcus antigen and two rabbits sensitized to horse serum were used. All animals were given injections of the antigen in the anterior chamber of the right eye, and at the same time a similar injection of salt solution in the anterior chamber of the left eye. The eye injected with the specific antigen showed the characteristic inflammatory reaction already described. The left eyes showed only a minor traumatic reaction. The eyes were thereafter kept under daily observation, and as soon as the inflammation began to subside in any given rabbit, further anterior chamber injections were given—the specific antigen in the right eye and sterile salt solution in the left eye. From five to six anterior chamber injections were required to maintain active inflammation. One rabbit was killed after 26 days and the remaining seven after 40 days of sustained inflammation.

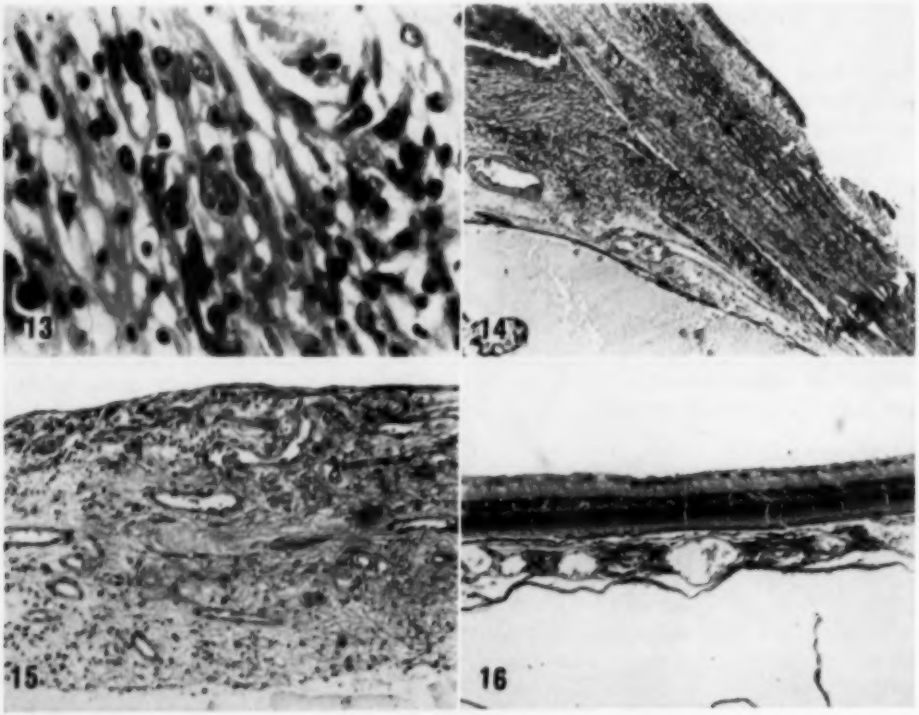
Controls. The left eyes of the test animals which received repeated anterior chamber injections of salt solution served as controls for the traumatic reaction. At the same time the hypersensitive animals were injected, two normal rabbits were given anterior chamber injections of streptococcus antigen and two other normal rabbits injections of horse serum. As further controls for the horse serum hypersensitivity reaction, two formerly sensitized rabbits which had been desensitized by the intravenous booster injection were given further repeated anterior chamber injections of horse serum.

Clinical course in test eyes. The degree of inflammatory reaction in the various rabbits ranged from "0.5" to "3.0." One rabbit, after one month of inflammation, was given a short remission. In the other seven test rabbits the inflammation was maintained without interruption.

During this prolonged period of inflammation the corneas became infiltrated and vascularized. This vascularization was usually deep in the stroma, and was quite unlike the superficial arborescent type usually seen in tuberculous eyes. Heavy inflammatory changes occurred in the iris, and some of the serofibrinous exudates in the anterior chamber became organized. One eye showed early buphthalmus at the time of death. There was no evidence of infection in any of the injected eyes, although it was evident at the last injection that the tissues were friable.

Clinical course in controls. The left eyes which received the salt solution injections showed only a minor evanescent traumatic reaction which subsided within 12 to 24 hours. At the conclusion of the experiment they appeared entirely normal. The eyes of the normal rabbits receiving repeated injections of bacterial antigens and horse serum, respectively, showed no reaction to the first two injections, but reacted to the third injection on the 12th day in the same manner as did the previously sensitized animals. The eyes of the two desensitized rabbits receiving repeated injections of horse serum showed minimal clinical reactions to each injection, but did not develop the organic changes shown by the hypersensitive animals, the animals apparently maintaining their desensitized status.

Histologic changes in test animals. The eyes of both groups showed almost exactly



Figs. 13-16 (Woods, Friedenwald, and Wood). (13) Same as Figure 12, high power. Lymphocytes, plasma cells, wandering cells. (14) Protracted allergic insult from repeated anterior chamber injections. Cellular infiltration of iris and angle. Organizing exudate in anterior chamber. (15) Protracted allergic insult from repeated anterior chamber injections. Scarring and monocellular infiltration of iris. (16) Protracted allergic insult from repeated anterior chamber injections. Collection of lymphocytes in anterior choroid—"choroiditis septica."

similar reactions, differing only slightly in severity. The corneas were edematous and were diffusely infiltrated with mononuclear wandering cells, lymphocytes, plasma cells, macrophages, and fibroblasts with scarring and vascularization, especially of the deeper layers (figs. 12 and 13). There were no nodular lesions except in relation to the puncture tracts of the injection, where occasional minute accumulations of lymphocytes and polymorphonuclear cells were to be found.

In the anterior chamber there was serum and abundant cellular exudation. In some instances there was beginning organization of the exudate (fig. 14). The irises were uniformly thickened, diffusely infiltrated with lymphocytes and plasma cells, with some beginning scarring (fig. 15). The ciliary body usually showed lesser inflammation of the same type, the reaction tapering off in the anterior choroid.

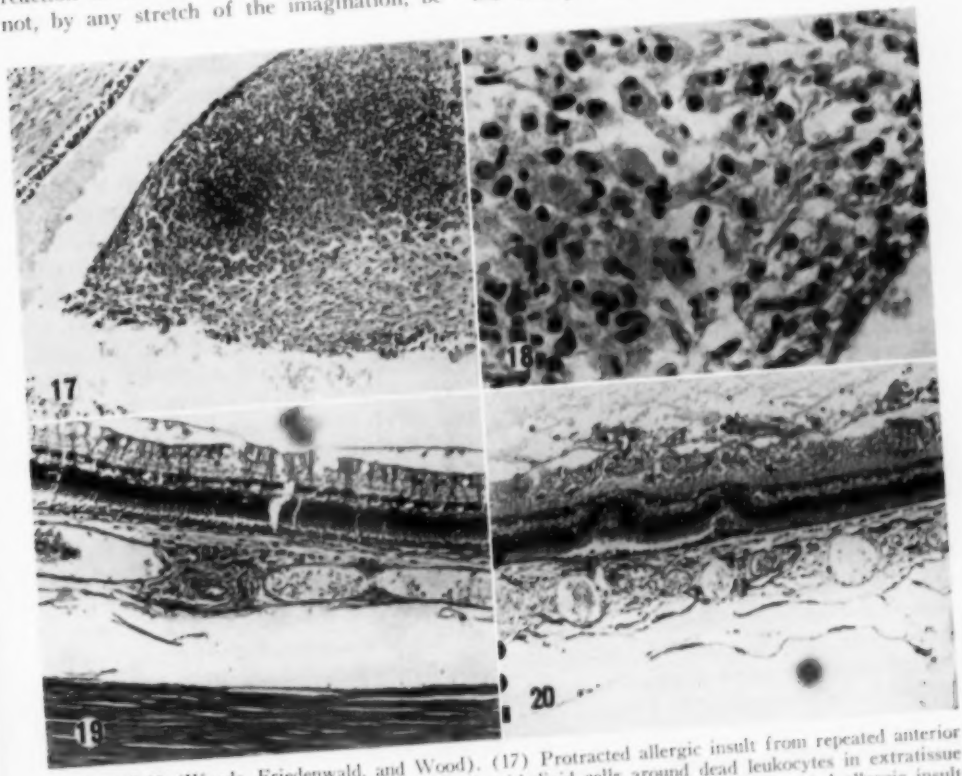
The posterior ocular tissues were essentially normal except for occasional scattered round cells in the choroid (fig. 16) corresponding to the picture of septic choroiditis. Since similar lesions were to be found in the fellow eye of one of these animals injected only with saline, this very mild choroidal lesion may be attributed to the general hypersensitivity reaction or to local mechanical trauma, but not to local administration of the antigen.

One of the rabbits sensitized to horse

serum and subjected to protracted anaphylactic inflammation showed an interesting finding. There was an organizing exudate of blood and fibrin in the anterior chamber. At the tip of this exudate, where it had apparently broken away from the angle wall, there was a small collection of large mononuclear macrophages and epithelioid cells (figs. 17 [low] and 18 [high]) around a mass of dead leukocytes. It was interesting that this small collection of epithelioid cells was the only such focus found in any of the sections and that it occurred, not in the fixed tissues, but in an exudate undergoing encapsulation. It was clearly a cellular reaction to the dead leukocytes, and could not, by any stretch of the imagination, be called a tuberculoid reaction.

In the group of eyes subjected to repeated bacterial allergic insult, no epithelioid cell nodules, or any other kind of nodular lesions were to be found, except those related to the puncture tracts noted above. The picture consistently corresponded to that of chronic nonspecific inflammation.

Histologic changes in the control eyes. The left eyes of the test animals which received only salt solution injection were almost free from any pathologic reactions. In some instances minute scars of the injection tracts were recognizable. In a few of these were isolated wandering cells in the iris and at the chamber angle. Reactions in the ciliary body were inconspicuous. One



Figs. 17-20 (Woods, Friedenwald, and Wood). (17) Protracted allergic insult from repeated anterior chamber injections. Collection of wandering and epithelioid cells around dead leukocytes in extratissue exudate (low power). (18) Ibid. High power, illustrating type of cell. (19) Protracted allergic insult from repeated anterior chamber injections—control eye. Collection of lymphocytes in anterior choroid—choroiditis septica. (20) Protracted allergic insult from intravitreal injection. Intense reaction on vitreal surface of retina.

animal showed slight, diffuse, round-cell infiltration of the choroid similar to that seen in the so-called "septic choroiditis" in man (fig. 19).

The normal animals which had received repeated intraocular injections of streptococcus antigens and horse serum, without preceding systemic sensitization, showed inflammatory reactions of the same type as the experimental group, though, in general, slightly less severe. The desensitized control eyes which received repeated anterior chamber injections of horse serum showed only minimal evidences of nonspecific inflammation.

EXPERIMENT III

Protracted hypersensitive reactions produced by repeated intravitreal injections.

Eight rabbits sensitized to streptococcus antigen and six rabbits sensitized to horse serum were used in this experiment. Intravitreal injections of the specific antigen were made in the right eye. The eyes were examined immediately after the first injection, and were kept under constant observation thereafter. If satisfactory lesions developed within four days after the first injection, the eyes were not reinjected as long as the lesions appeared active and progressive. Rabbits which did not develop progressive lesions were re-injected as soon as it became evident the lesions were inactive or regressive. Thus, two of the rabbits sensitized to streptococcus received only one intravitreal injection, and six received three injections 11 to 12 days apart. One of the rabbits sensitized to horse serum received two intravitreal injections, two received three injections; and the remaining three were given four, five, and six injections, respectively. The interval between the injections varied from three to 10 days.

One rabbit sensitized to streptococci was killed on the fifth day after one intravitreal injection in order to study the histology of the early lesion. One horse serum rabbit was similarly killed on the 28th day after two injections. The remaining 12 rabbits were killed on the 43rd day.

Controls. As controls for the trauma of injection, at the time the specific antigen was injected in the right vitreous, a like amount of sterile saline was similarly injected in the left vitreous. As additional controls, two normal rabbits were each given one intravitreal injection of streptococcus antigen, and two other normal rabbits were given one intravitreal injection of horse serum at the same time the test rabbits were first injected with the specific antigen.

All animals were tested for a hypersensitivity prior to death and all were found hypersensitive.

Clinical course in test eyes. Immediately after the intravitreal injection the eyes of all animals showed a slight haze in the vitreous, but were otherwise normal. At the end of 24 hours all of the rabbits sensitized and injected with horse serum showed well-marked fundus lesions. The rabbits sensitized and injected with streptococci showed more delayed reactions. One rabbit showed a fundus lesion at the end of 24 hours, four showed lesions at the end of 48 hours, two did not show a fundus reaction until the fifth day, and one did not develop visible lesions until the 13th day after the first intravitreal injection. The lesions in the rabbits sensitized and injected with streptococci were perhaps more chronic than those in the group sensitized and injected with horse serum. With these exceptions—delayed and possibly more progressive lesions in the streptococcus rabbits—the clinical picture and course of the lesions was the same in the two groups.

The reaction was confined entirely to the posterior ocular segment. There was practically no evidence of anterior uveal inflammation. The first change noted was an increasing vitreous haze, quickly followed by exudates in the fundus. Occasionally these exudates were focal in type, but as a rule they were diffuse and spread over a large portion of the fundus. In a few rabbits they

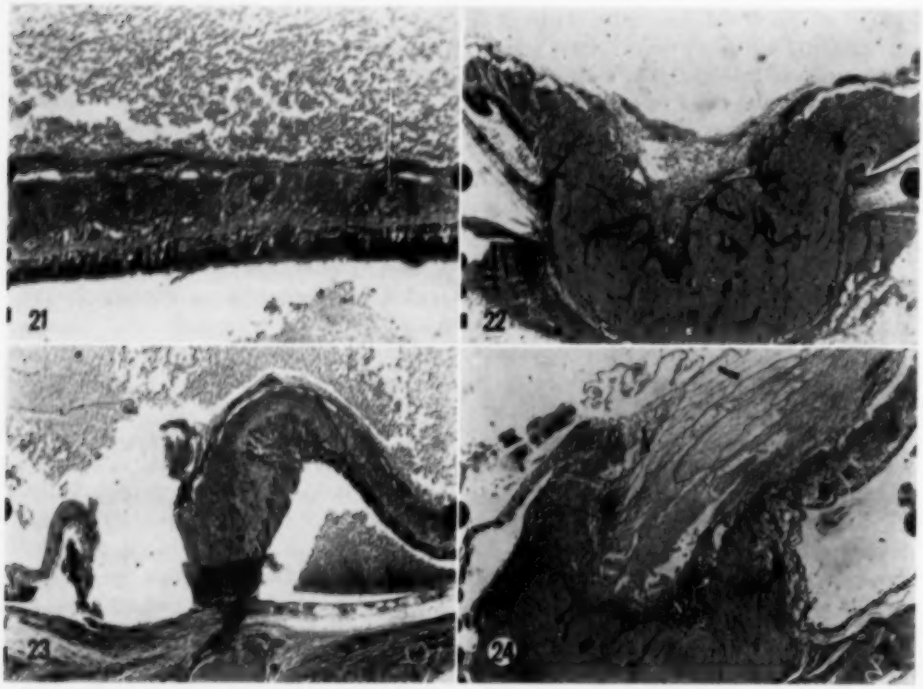
were so extreme that the entire red reflex was lost, and all that could be seen was a diffuse whitish veil over the entire retina. In a few advanced cases an obvious separation of the retina could be made out, but in the majority it was impossible to tell whether the retina was actually detached or not. There was a conspicuous absence of hemorrhage. In some of the rabbits, especially those injected with horse serum, the reaction would become markedly aggravated after each injection, then would appear to regress after three or four days, to be reactivated by further intravitreal injections.

Clinical course in controls. The left eyes of the test rabbits injected with salt solution showed practically no reactions of any kind other than an occasional small focal exudate in the fundus. The normal rabbits, which received one intravitreal injection of horse serum, showed no reaction of any kind until the 10th and 12th day after the injection. They then developed the vitreous haze and fundus lesions similar to the previously sensitized animals. In one rabbit this progressed to a maximum of "1" by the third day, and then slowly regressed until there was only a trace of reaction at the time of death, while the second rabbit developed a fundus lesion which progressed up to a detached retina. One of these rabbits gave a violent skin test to horse serum at the time of death, and the other a very doubtful or negative test. The eyes of the normal rabbits which received the intravitreal injection of streptococcus antigen remained negative up to the 12th day, and then developed mild exudative fundus lesions which persisted up to the time of death. Both rabbits then gave positive tests to an intracutaneous injection of vaccine, a hypersensitivity manifestly having developed as a result of the one intravitreal injection.

Histology of the test eyes. The two groups of rabbits showed in general the same histologic changes, with the exceptions that the lesions shown by the rabbits sensitized and injected with horse serum were more intensely exudative than those shown by the streptococcus group, and in the horse serum group there was one rabbit which showed a granulomatous type change. The general patterns of the usual lesions were as follows:

The anterior ocular segments (cornea, anterior chamber, and iris) were uniformly negative, or, at most, showed a few mononuclear wandering cells at the chamber angle. The retinas were edematous, infiltrated with wandering cells, and in many eyes were detached. The inflammation was most intense on the vitreal surface of the retina (fig. 20), which was often covered with a serous exudate in which were enmeshed many lymphocytes and macrophages (fig. 21). At the posterior pole the inflammation increased and was particularly prominent perivascularly at the optic disc (figs. 22 and 23). The optic disc was usually swollen, and was covered with an organized exudate with numerous wandering cells and new blood vessels. The combination of papilledema, inflammatory exudate, a proliferating retinopathy with detachment, at times limited to the peripapillary region, made these tissues project like a hillock in the vitreous cavity (fig. 24).

There were wandering cells in the subretinal fluid where the retina was detached, and there was a choroidal infiltration of varying intensity, chiefly of lymphocytes, plasma cells, and large mononuclears (fig. 25). There were no epithelioid cell nodules, although an occasional isolated epithelioid cell could be recognized. The choroidal invasion was sometimes diffuse (fig. 26) and sometimes focal (fig. 27). The focal infiltrates were found most often in the peripapillary region and at the ora. When the retina was detached, this cellular infiltration was often particularly marked under the pigment epithelial layer. There again, the infiltration was sometimes diffuse and sometimes nodular. When nodular (fig. 28), it resembled in its gross configuration the Dalen-Fuchs nodules of sympathetic oph-



Figs. 21-24 (Woods, Friedenwald, and Wood). (*21*) Protracted allergic insult from intravitreal injection. Serous exudate in vitreous. (*22*) Protracted allergic insult from intravitreal injection. Perivasculitis, papillitis, and edema of disc. (*23*) Protracted allergic insult from intravitreal injection. Proliferatory retinopathy, edema, subretinal exudate, and retinal detachment near papilla. (*24*) Protracted allergic insult from intravitreal injection. Proliferated and infiltrated retina projecting from papilla into vitreous.

thalmia, but it differed sharply from them in the absence of epithelioid cells, giant cells, and pigment phagocytosis, being composed chiefly of lymphocytes and plasma cells (fig. 29). The pars plana of the ciliary body participated in the retinal and choroidal inflammation, but the anterior portion of the ciliary body showed little reaction.

In one eye, from a rabbit sensitized and re-injected with horse serum, there was a unique finding. This consisted in a broad sheet of epithelioid and giant cells arranged in a palisade on the surface of the choroid under the detached retina (fig. 30 [low] and fig. 31 [high]). This palisading resembled that seen in rheumatoid lesions in man, where, however, it is usually found surrounding necrotic collagen.

Histologic changes in controls. The left eyes of the test rabbits, injected intravitreally with salt solution, were entirely normal, with the exception of one suprachoroidal hemorrhage encountered near a puncture hole.

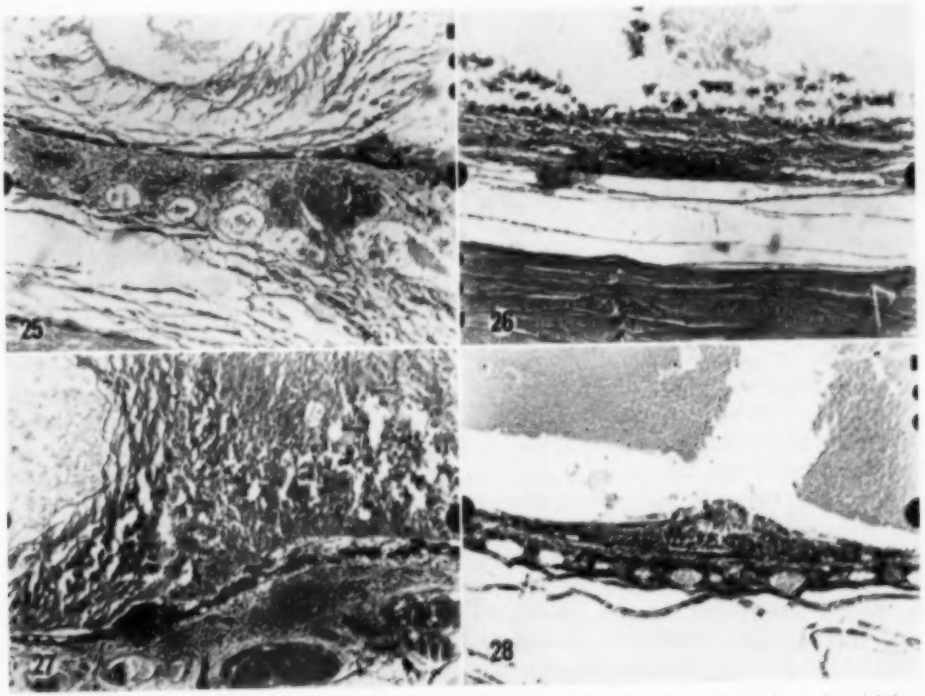
The right eyes of the normal rabbits which received one injection only of horse serum and streptococcus antigen, respectively, showed moderate reactions of the same type shown by the previously sensitized rabbits.

Comment

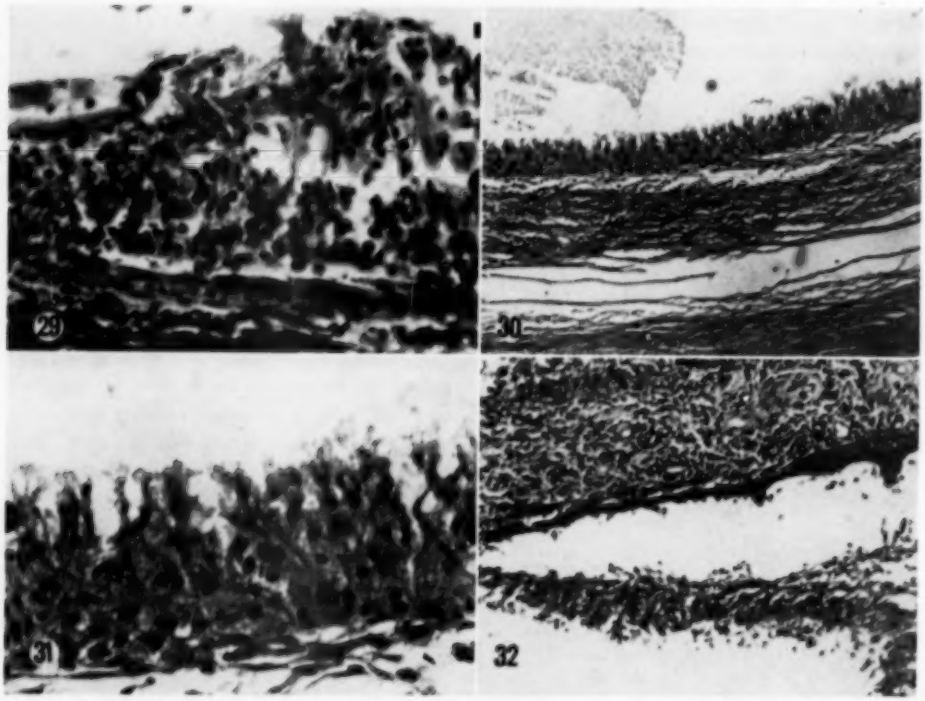
In these experiments there were only insignificant differences in the clinical and histologic pictures of the ocular hypersensitive reactions caused respectively by protein and bacterial antigens. The only difference noted in the clinical reaction was that in the rabbits sensitized and re-injected with the

horse serum, inflammation occurred more promptly and was somewhat more evanescent than in the rabbits sensitized and reinjected with the bacterial antigen. Similarly, the histologic picture of exudation was more intense in the horse-serum rabbits than in the streptococcus group. The more prompt and intense exudative reaction in the horse serum group may be due to the fact that the horse serum was more readily absorbed, or it may be due to a fundamental difference in the mechanism of the anaphylactic (protein hypersensitivity) and the allergic (bacterial hypersensitivity) reactions. While there is considerable difference in the cutaneous reactions of anaphylactic and bacterial hypersensitivity, in the eye there was little clinical or histologic difference between these two forms of the hypersensitive reaction.

A second minor point of interest was the delayed reactions which occurred in the eyes of the control rabbits in Experiment II. These previously insensitive eyes received repeated anterior chamber injections. They showed no reaction to the first and second injections, but showed typical hypersensitive reactions to the third injections about the 12th day. Similarly, the normal rabbits receiving intravitreal injections in Experiment III reacted on the 12th day without further insult. In both cases these delayed reactions were clearly hypersensitive phenomena, in the first instance due to a sensitization from the first injection and a reaction of the sensitized tissue to a later injection of the



Figs. 25-28 (Woods, Friedenwald, and Wood). (25) Protracted allergic insult from intravitreal injection. Diffuse and nodular lymphocytic infiltration of choroid. (26) Protracted allergic insult from intravitreal injection. Focal lymphocytic infiltration of choroid. (27) Protracted allergic insult from intravitreal injection. Advanced focal lymphocytic infiltration of choroid with subretinal serous exudate. (28) Protracted allergic insult from intravitreal injection. Focal collection of cells beneath pigment epithelium, resembling Dalen-Fuchs nodule.



Figs. 29-32 (Woods, Friedenwald, and Wood). (29) High-power view of Figure 28, illustrating nature of cells—lymphocytes and plasma cells. (30) Protracted allergic insult from intravitreal injection. Palisade of epithelioid cells over choroid, beneath detached retina. (31) Ibid. High power illustrating epithelioid cells. (32) Chronic nongranulomatous iritis in human—low power—illustrating palisade of epithelioid cells beneath iris.

same antigen. In the second instance it was due to sensitization from the first injection and a reaction of the sensitized tissue to unabsorbed antigen remaining in the adjacent vitreous gel—the same general mechanism as that of serum sickness.

The first important point demonstrated by these experiments is that, in general, the hypersensitive reaction in the eye follows a definite pattern. After an acute insult, there is an outpouring of leukocytes which are soon replaced by lymphocytes and their transition forms, plasma cells. If the insult is short and not repeated, there is a quick recovery. If the insult is protracted and intense, the cellular reaction is marked, and there is a general infiltration of the tissues. Macrophages arrive on the scene and go about their routine business of policing up the premises, ingesting and removing dead leukocytes, necrotic tissue, and foreign material. While they may progress into their transition form of epithelioid cells, these cells do not form nodules or tubercles. When the hypersensitive insult is still further prolonged, there are diffuse and nodular collections of mononuclear cells, lymphocytes, and plasma cells throughout the choroid—the usual picture of chronic inflammation. Under the extraordinary conditions which prevailed in Experiment III, where relatively immense amounts of antigen were imprisoned in a gel to which the encompassing hypersensitive tissues were constantly exposed, proliferative changes took place in the exposed retina. This is the picture of

nonspecific inflammation, does not resemble tuberculoid or granulomatous lesions, and can readily be differentiated from such.

The second important point was the isolated finding of a palisade of epithelioid cells over the infiltrated choroid in one eye subjected to this intense and prolonged allergic insult. This picture was quite similar to the palisading observed in a rheumatic nodule, and which Rich observed about a bit of degenerating collagen in the heart valve of an animal with experimental periarteritis nodosa. However, there was no evidence of degenerating collagen or necrotic material in this eye, which would thus explain the palisading epithelioid cells.

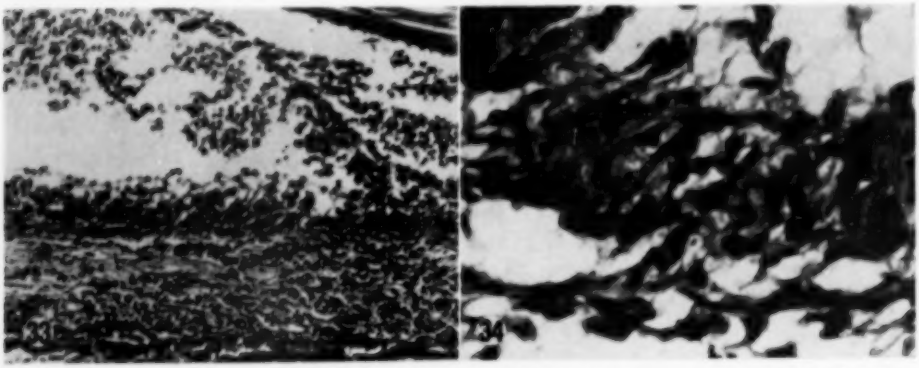
In 1952, Rich found typical tuberculoid reactions and sheets of epithelioid cells around the Malphigian bodies of the spleen in animals with experimental serum sickness and periarteritis nodosa. He suggested at that time that this reaction might be the result of a condition which allowed antigen to be present in the circulation after antibody had formed. We investigated this possibility in one of these experiments.

In Experiment II, the rabbits previously sensitized to horse serum were given 15 cc. of horse serum intravenously before the eyes were injected. Several of the animals died of anaphylactic shock, but four survived. Two of these were completely desensitized by the intravenous injection, but the other two remained highly hypersensitive. The eyes of the hypersensitive rabbits, with antigen circulating in the blood stream, were later injected repeatedly with horse serum. They showed only the usual clinical reaction and the histologic pictures of nonspecific inflammation. There were no tuberculoid changes or aggregations of epithelioid cells.

To explore further this suggestion of Rich's, two normal rabbits were given two injections of horse serum in the anterior chamber, and 10 days after the first injection, when antibody was beginning to form, were given 15 cc. of horse serum intravenously. Both rabbits survived and were later given a third anterior chamber injection of horse serum. These rabbits showed the usual clinical picture of the ocular hypersensitive reaction and the histologic picture of nonspecific inflammation. The serum of all four of these rabbits gave positive precipitin tests against the serum of an animal immunized to horse serum, showing clearly that specific antigen was still free in their circulation. In these animals, with antigen circulating in the blood stream after the formation of antibody, there were no epithelioid cell or tuberculoid reactions. There must therefore be some factor other than circulating antigen which precipitates epithelioid cell palisading and tuberculoid changes in the hypersensitive inflammatory reaction.

We suspected that this precipitating factor might be a secondary infection of some sort, just as we similarly suspected some granulomatous disease in the experiment reported by Schlaegel and Davis. However, a review of the record and the autopsy of this rabbit showed no evidence of any secondary infection. Bacterial strains of the affected eye did not reveal either bacteria or fungi in the tissue. We are therefore forced to conclude that this peculiar inflammatory picture, like that of the rheumatoid lesions which it resembles, represents an unusual form of chronic allergic reaction.

It should be pointed out that this sheet of palisading epithelioid cells is not the same thing as a tubercle or a tuberculoid reaction, and that the lesions in granulomatous uveitis are readily distinguishable under the microscope from this peculiar "rheumatoid" lesion. In fact in the whole pathologic collection of the Wilmer Institute (over 15,000 specimens) an intraocular inflammation with intense epithelioid cell palisading has only once been encountered (figs. 32, 33, and 34). This was in a case of unilateral iritis following cataract extraction on the other eye, a case in which the available clinical record cast little light on the nature of the lesion, but which, in the light of our present experi-



Figs. 33 and 34 (Woods, Friedenwald, and Wood). (33) Chronic nongranulomatous iritis in human—low power—illustrating palisade of epithelioid cells over iris in anterior chamber. (34) Ibid. High power, illustrating epithelioid cells.

ments, may now be classified as a peculiar form of chronic allergic inflammation.

Summary

The results of a study of the histopathology of the ocular hypersensitive reaction are reported. Both bacterial and foreign protein antigens were used for sensitization and re-injection. Single acute allergic reactions were produced by one anterior chamber injection and prolonged allergic inflammation was produced by repeated anterior chamber and intravitreal injections of the specific antigen in the eyes of sensitized rabbits.

In general, more prompt, acute, and somewhat shorter reactions were produced by foreign protein (horse serum) antigens than were produced by bacterial antigens. Except for this slight difference, horse serum and bacterial antigens produced the same clinical response and histologic picture in both the acute and the chronic reactions.

The general histopathologic picture was that of nonspecific inflammation. The immediate allergic response is the outpouring of leukocytes. These are soon replaced by lymphocytes, plasma cells, and a few wandering cells. In acute reactions these disappear within one week and the eyes return to normal. In the chronic reaction there is a cellular infiltration of the tissues with lymphocytes, plasma cells, and wandering cells. This infiltration may be diffuse or nodular. When nodular, it may assume the picture of chronic inflammation with nests of lymphocytes and plasma cells, and when such collections occur beneath the pigment epithelium, they resemble grossly the Dalen-Fuchs nodules of sympathetic ophthalmia. However, they are made up of lymphocytes and plasma cells, and not of epithelioid and giant cells. In the retina there is perivasculitis, and secondary proliferating changes.

Tuberculoid lesions did not occur. However, in one rabbit subjected to prolonged allergic inflammation, a nest of epithelioid cells phagocytosing dead leukocytes was found in an extratissue exudate. In another rabbit, a sheet of palisading epithelioid cells was found over the choroid beneath a detached retina. This resembled somewhat the so-called rheumatic nodule reaction. No explanation could be found for this unique finding and it was believed it represented a peculiar form of chronic allergic inflammation.

Conclusions

1. The ocular reaction which follows either a single or repeated allergic insult, follows the general pattern of nonspecific inflammation.

2. Tuberculoid or granulomatous reactions were not found in eyes subjected to either acute or prolonged allergic inflammation. In one eye only, a sheet of palisading epithelioid cells was found. This suggested the reaction found in a rheumatic or rheumatoid nodule. No obvious explanation could be found for this, and it was concluded it represented a peculiar form of chronic allergic inflammation.

3. There was no essential difference in the ocular reaction produced in specifically sensitized animals by foreign protein or bacterial antigens.

The Johns Hopkins Hospital (5).

REFERENCES

1. Woods, A. C.: Endogenous uveitis. Tr. 17th Internat. Congress Ophth. 1954 (in press).
2. Rich, A. R.: Hypersensitivity to iodine as a cause of periarteritis nodosa. Bull. Johns Hopkins Hosp., **77**:43, 1945.
3. Van Wyk, J. J., and Hoffman, C. R.: Periarteritis nodosa: A case of fatal exfoliative dermatitis resulting from "Dilantin sodium" sensitization. Arch. Int. Med., **81**:605, 1948.
4. Rich, A. R., and Gregory, J. E.: Further experimental cardiac lesions of the rheumatic type produced by anaphylactic hypersensitivity. Bull. Johns Hopkins Hosp., **75**:115, 1944.
5. Rich, A. R.: The occurrence of focal tuberculoid lesions in experimental serum sickness. Bull. Johns Hopkins Hosp., **91**:109, 1952.
6. Schlaegel, T. F., and Davis, J. B.: Reaction of rabbit eye to normal horse serum: Sensitization by intradermal injection. Am. J. Ophth., **26**:785, 1943.
7. Biegel, A. C.: Effect of cortisone on horse-serum uveitis in rabbits. Arch. Ophth., **45**:256, 1951.
8. Woods, A. C., and Burky, E. L.: Experimental studies of ocular tuberculosis. I. Relation of ocular sensitivity to cutaneous sensitivity in the systemically infected rabbit. Arch. Ophth., **19**:229, 1938.

AN EVALUATION OF THE TUBERCULIN REACTION IN ENDOGENOUS UVEITIS*

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Tuberculous uveitis is a rather frustrating and elusive disease entity. It cannot be diagnosed with assurance; nearly always the diagnosis must be made by presumption and by elimination. The time-honored tuberculin test is of help only in a negative sense. Although a negative reaction in a patient with uveitis rules out, for all practical purposes, the possibility of a tuberculous etiology, a positive skin test to tuberculin gives little or no diagnostic help.

In such circumstances it is not surprising that estimates of the importance of tuberculosis in the causation of uveitis show wide disparities. Thiel,[1] for example, in a review of all cases of endogenous uveitis seen over an 18-year period in Frankfort, Germany, concluded that 75 percent of the cases were tuberculous in origin. Amsler,[2] in Switzerland, has stated that tuberculosis is an important factor in at least 10 percent of cases of chronic uveitis and that it plays a probable or possible role in 40 percent of cases. Figures such as these serve to explain the feeling that tuberculosis may well be a fairly common factor in the causation of uveitis.

On the other hand, it is well known among tuberculosis specialists that eye complications are rare in patients with active tuberculosis, and Fritz,[3] in a study of 2,000 Alaskan native children, did not encounter a single case of typical endogenous uveitis, despite the fact that the children were almost universally affected with tuberculosis as evidenced by tuberculin testing and by a high incidence of pulmonary and extrapulmonary tuberculosis.

* From the Wills Eye Hospital.
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If tuberculosis is an etiologic factor in a significant number of cases of endogenous uveitis, it would seem reasonable to anticipate that a statistically higher percentage of positive reactors to tuberculin would be found in patients with uveitis as compared with a normal control group. Our present study stems from this thesis and is an attempt to evaluate the possible role of tuberculosis in uveitis by a comparative analysis of tuberculin reactions.

Method

The records at the Wills Eye Hospital since 1949 were reviewed, and all cases of inflammatory disease of the uveal tract in which tuberculin tests had been done were collected. Cases of traumatic uveitis, postsurgical uveitis, and sympathetic ophthalmia were excluded. A total of 499 cases was obtained. Of these, 440 cases came from the wards; 284 of the ward group were white patients and 156 were Negroes. Private cases numbered 59; of these, 57 were white patients.

The 499 cases of endogenous uveitis were broken down into 10-year age groups according to the age of the patient when first seen. In addition, the cases were divided into those occurring in white patients and those occurring in Negro patients. These subdivisions were necessary because, in the general population, the frequency of positive tuberculin reactions increases from infancy to adult life and because positive tuberculin reactions are felt to be somewhat more common in colored individuals than in white individuals of comparable age group.

As controls, a group of 197 patients were tuberculin tested with PPD. These patients came from the refraction clinic and from the wards and did not have inflammatory disease of the uveal tract. Both the uveitis and the control groups, except for the 59 private uveitis cases, came from the same socio-economic environment and from the same geographic area, and thus meet the basic requirements for comparison. We were surprised to find in the course of this study that no published survey of tuberculin reactions of a large unselected general population is available—such a survey might have provided an additional control group.

For comparative analysis, the percentage of positive reactors to the first strength of PPD and the percentage of positive reactors to either the first or the second strength of PPD were plotted by decades.

Results

Figure 1 shows the percentages of positive reactors to PPD by decades among the white ward uveitis patients and the Negro ward uveitis patients. The lower pair of curves demonstrate that the frequency of positive reactions to first strength PPD is slightly higher in the Negro group. The same finding is apparent, with the exception of the 40 to 49 age group, in the reactions to either first or second strength tuberculin as shown in the upper pair of curves.

Figure 2 shows the percentages of posi-

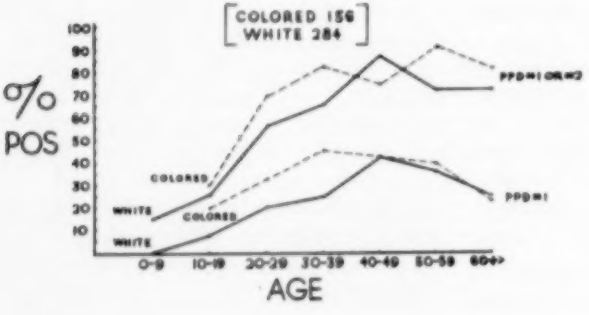

Fig. 1 (Hanno and Spaeth). Tuberculin reactions in ward patients with uveitis.

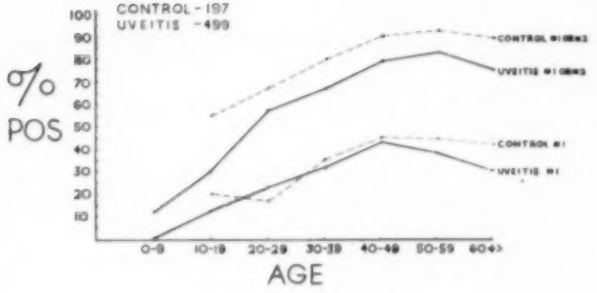

Fig. 2 (Hanno and Spaeth). Tuberculin reactions in uveitis.

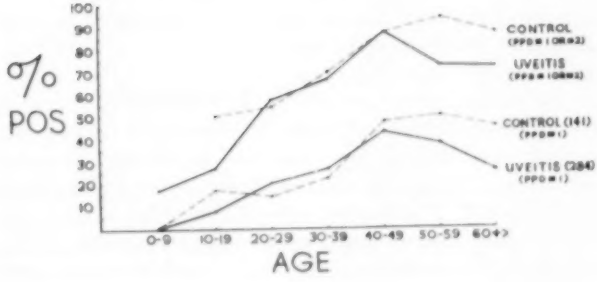

Fig. 3 (Hanno and Spaeth). Tuberculin reactions in white ward patients.

tive reactors to PPD in our 499 cases of uveitis and compares them with the findings in the control group of 197 individuals without inflammatory uveal tract disease. As far as race is concerned, both groups are analogous: 31.5 percent of the uveitis group and 28.4 percent of the controls are Negro. With regard to the first strength reactions, shown in the lower pair of curves, the uveitis and control groups are quite similar. In the case of the positive reactors to either first or second strength tuberculin, represented by the two upper curves, the control group in each decade shows a slightly higher percentage of positive reactors than the uveitis group.

Figure 3 shows the percentages of positive reactors by decades in our group of 284 white ward uveitis cases as compared with the findings in the group of 141 white controls. The two sets of curves show no significant difference. A similar chart could not be made for the Negro uveitis patients and the Negro controls because of the relatively small number of Negro controls which we were able to obtain.

Summary

The percentages of positive reactors to PPD, grouped according to 10-year age groups and color, in a series of 499 patients with endogenous uveitis were compared with the corresponding percentages of positive reactors in a control group of 197 patients without inflammatory disease of the uveal tract.

The results demonstrate that the uveitis population did not show a higher than normal percentage of positive reactors to tuberculin.

This strongly suggests that tuberculosis cannot be an etiologic factor in a significantly large percentage of cases of endogenous uveitis.

1930 Chestnut Street (3).

REFERENCES

1. Thiel, R.: Cited by Kimura, S. J., Hogan, M.J., and Thygeson, P.: Uveitis in childhood. Arch. Ophth., **51**:80, 1954.
2. Amsler, M.: L'uvéite chronique. Bull. Soc. ophtal., France, **4**:407, 1952.
3. Fritz, M. H.: Cited by Kimura, S. J., Hogan, M. J., and Thygeson, P.: Uveitis in childhood. Arch. Ophth., **51**:80, 1954.

CYCLODIATHERMY: RESULTS IN VARIOUS TYPES OF GLAUCOMA*

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In the treatment of glaucoma, a new era had its beginning in the 1930s with the use of diathermy by the ciliary-body approach. As early as 1932, Weve[1] employed surface diathermy of the ciliary region in the treatment of infantile glaucoma. This method was later emphasized by Albaugh and Dunphy,[2] and Weekers[3] used much the same technique. In 1936, Vogt[4] first described the use of perforating cyclodiathermy in glaucoma. His original technique consisted of as many as 100 punctures in three rows, the closest row placed 2.5 mm. from the limbus, over a band extending one third to one half of the circumference of the globe. He employed a needle 0.5-mm. long in phakic eyes and 1.0-mm. long in aphakic eyes, applying it to the bare sclera. The procedure was in his opinion the operation of choice in cases of glaucoma in which all other surgical and medical measures had failed, and in glaucoma secondary to uveitis.

The literature on the subject of cyclodiathermy is copious, for the subject has remained controversial. Too, techniques have varied. In the early days the operation consisted of perforation, partial perforation, or surface coagulation up to 2.5 to 4.0 mm. from the limbus. In due time, numerous papers appeared in the literature, both in praise and in condemnation of the Vogt method. By the late 1940s, the use of cyclodiathermy was on the wane "because of its unpredictable effect upon ocular tension and the high incidence of corneal opacity, probably due to damage to the cornea by the diathermy current."[5]

THE NEW TECHNIQUE

At midcentury the literature stressed the probability that the intraocular pressure might be lowered through changes produced in the ciliary nerves or by diminution of the blood supply of the ciliary body with subsequent atrophy. Reiser,[6] therefore, advocated placing the punctures 8.0 mm. from the limbus and was most careful to cauterize the insertion of the muscles in order to close off the ciliary arteries. Other authors[7,8] soon emphasized placing punctures well back. Arruga[9] also believed the operation to be effective through its action upon the ciliary nerves and accordingly directed his cautery to the region of the tendons of the rectus muscles overlying the long ciliary nerves and arteries. He applied a 1.0-mm. electrode for five to 15 seconds and used 15 to 20 applications through the conjunctiva about 9.0 mm. from the limbus. Later, in the 1952 edition of his textbook,[10] he gave an excellent description of the operation.

In 1951, Castroviejo[11] described a technique differing from that of Arruga,[9] in which he made eight to 10 punctures over half the globe, 6.0 mm. back from the limbus, using a 1.0-mm. needle and applying the electrode for 10 seconds at each application. Occasionally, he encircled the entire globe. Enthusiastic about the use of this procedure, he employed it for all types of glaucoma. At my last observation of his surgery, in his

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controlled diathermy he was employing transconjunctival punctures and, after air injection into the anterior chamber, repeating the procedures if the tonometric readings warranted.

Largely through the work of Castroviejo[11] in this country and Weekers[3] in Europe, cyclodiathermy by 1951 was beginning to enjoy a second wave of popularity. In his review of the literature on glaucoma for 1952-1953, Haas[12] observed a decided tendency to move the site of diathermy posteriorly so that the electrocoagulations are made 7.0 to 9.0 mm. from the limbus. Neubauer[13] modified the operation by placing surface diathermy just in front of the external rectus muscle, thereby creating a partial obliteration of the branches of the long ciliary arteries. He reported success in 63 percent of cases. Araló[14] employed a similar procedure, using 1.5-mm. perforating electrodes, and encountered no complications. It was his belief that the operation is indicated in chronic glaucoma and as a supplementary procedure in congenital glaucoma and in aphakic glaucoma.

Scheie,[15] who in mid-1949 had discontinued use of the Vogt technique because of its "erratic effect" on intraocular pressure and "frequent corneal damage," resumed the performance of cyclodiathermy early in 1951 after being influenced by Castroviejo's enthusiasm for the newer technique employed in Europe. In July, 1952, he reported his experience with the Vogt technique in an early group of cases and with the newer method in a later group, and concluded that the newer technique appeared to be useful in situations in which other operative procedures had failed and in advanced glaucoma. One year later, in discussing a paper by Lachman and Rockwell,[16] he observed that the present-day techniques, as suggested by Castroviejo[11] in this country and Weekers[3] and Reiser[6] in Europe, all recommend application of the current 6.0 mm. or more from the limbus and that in his experience at the Hospital of the University of Pennsylvania "the newer technique has proved to be quite safe." He declared also that he had encountered no serious complications, as with the older technique, and none of those mentioned by the authors who had complained that the results of perforating cyclodiathermy by Castroviejo's method are unpredictable and the procedure not entirely safe.

Since the reversal in technique which has limited the perforating procedure to a distance of 6.0 mm. from the limbus, ranging out to 11 mm., the average distance in my work has been 6.0 to 9.0 mm. from the limbus. Although my 10 years' experience with the procedure includes the earlier period in which it was the practice to make diathermic applications too close to the limbus, in my hands this newer therapy has been safe. Certainly, an eye subjected to an operation of this type does not pose the later difficulties of extracting the lens through a filtering wound, nor does it present the difficulty sometimes experienced even with a preliminary iridectomy.

The technique I have worked out is as follows:

In adults, local anesthesia is usually employed, and in children general anesthesia. Not much topical anesthesia is used because of the danger of devitalizing the cornea. After adequate anesthetization, particularly in the muscle cone, an incision is made in the conjunctiva from the lower border of one of the horizontal muscles to that of the other 6.0 mm. from the limbus. The inferior rectus is exposed, and the tendon is picked up on a hook. The sclera is bared both in the temporal and nasal quadrants, and the globe is kept constantly elevated with the hook. Accurate marking is made on the sclera 8.0 mm. from the limbus in each quadrant, and the coagulation begins from there.

Usually the punctures number about 30 on a 6.0- and on an 8.0-mm. arc, with at least 15 in each lower quadrant of the bare sclera. In some cases, the number of coagulations is increased, and they are placed out

as far as 9.0 to 11 mm. and in as close as 6.0 mm., with as many as 25 in each quadrant.

It is my practice to make certain that there is vitreous presentation in a few punctures when the intraocular pressure is especially high and also to reduce the pressure when cyclodiathermy is combined with an intraocular procedure such as a cataract extraction or an iridectomy.

In case a second operation is desirable, it is performed above. The same method is utilized as in the lower quadrants, with a hook placed under the superior rectus, pulling the globe down. If a third operation is attempted, it is performed immediately in front of and behind the insertion of the internal and external recti to affect the region of the long ciliary vessels. Of late I have given more attention to the area about the insertion of these muscles, aiming for the effect on the long ciliary vessels and nerves.

A 1.0-mm. electrode is used, and the current is determined which will produce a browning of the sclera. The applicator is not kept in contact more than four seconds at any time and usually two to three seconds. At all times an effort is made to keep a dry field, and the greatest surgical respect is paid to the cornea.

In adults, the conjunctiva usually is closed with a running 6-0 silk suture, and in children an absorbable plain catgut suture is used. Eserine ointment and antibiotic ointments are used in the operated eye or eyes. Both eyes are padded even though the procedure is only monocular.

The technique of cyclodiathermy is relatively simple and is being improved. A surgeon with limited experience can perform it with safety. The speed of the punctures, in my opinion, does not have to be controlled. In personal observation, however, of the surgery for retinal separation performed by Dr. Dohrmann K. Pischel, I noted that if the cornea showed any tendency to cloud because of elevated intraocular pressure in the course of diathermic applications, he retarded the speed of the punctures and also cooled the eye by means of saline irrigation. In three cases I have observed a rather rapid rise of intraocular pressure during surgery as shown by indenting the globe and corneal clouding. Following the immediate use of eserine ointment postoperatively, no significant complications developed.

The results of cyclodiathermy in congenital glaucoma in my hands[17] have been highly gratifying, both when it was used alone and in combination with goniotomy. A detailed report of this group of my cases is now in process of preparation.

In a group of cases with associated retrolental fibroplasia, vitreous dysplasia, and often microphthalmos, cyclodiathermy is in my opinion the operation of choice. I have had one case of aniridia in which treatment with cyclodiathermy was successful.

In three cases of glaucoma associated with rubeosis iridis diabetica this operation has proved successful in my hands. In one of these cases there was an associated thrombosis of the central vein. In reporting a case, deRoetth[18] concluded that cyclodiathermy is the only procedure thus far found to lower the intraocular pressure in cases of glaucoma associated with rubeosis iridis diabetica.

I have been impressed with the efficacy of this procedure in glaucoma occurring in Negroes. Among them the disease has frequently presented a problem difficult to solve, for treatment by any method has proved much less satisfactory in this race. For the control of intraocular pressure in Negro cases in my experience, prior to cyclodiathermy it had been necessary to combine an iris inclusion operation with a corneosclerectomy. Cyclodiathermy was employed successfully in 27 of the 33 cases occurring in Negroes in the series of cases reported here, the results comparing favorably with those in white patients.

My results with cyclodiathermy in aphakic glaucoma have been good. I now can concur in the opinion of Arató[14] that this therapy is indicated for glaucoma in aphakia. In the

present series it was successful in 11 of 14 eyes.

Analysis of cases

A series of 80 cases in which cyclodiathermy was performed one or more times is reported and the individual cases are summarized in Table 1. There were 47 white and 33 Negro patients in the series. The age of the youngest patient was 15 months and of the oldest patient 83 years, the average being 55 years. Cyclodiathermy was performed 141 times in 120 eyes; it was repeated once in 17 eyes and twice in two eyes.

The series covers a period of five years from mid-1949 to mid-1954. Prior to December, 1952, there were 36 cases, in almost all of which the punctures were made 6.0 mm. or less from the limbus. In the 44 cases since that time, the newer technique has been employed consistently with the distance from the limbus increased to 6.0 to 10 mm. The results, which have improved appreciably with the newer technique, are tabulated in Tables 2 to 6.

After discussing the matter with many ophthalmic surgeons, I have concluded that the upper limit of normal in glaucomatous eyes should be 30 mm. Hg. Apparently, the majority of these eyes with long-standing disease will respond well if the basic pressure is maintained around this level without progressive deterioration of the visual acuity and restriction of the fields. Accordingly, I have classified results in this series on this basis. It is to be remembered in evaluating results in cases of this type that successful therapy varies with the individual case. In one instance control of intraocular pressure may mark success whereas in another avoiding enucleation may be its measure.

Eight cases are described to illustrate the use of cyclodiathermy in various types of glaucoma. In six of these cases this therapy was successful and in two unsuccessful.

Report of cases

Case 19

Chronic noncongestive open-angle glaucoma in a Negro. R. J., a Negro, aged 30 years, was referred by Dr. Arthur R. Beyer of Tampa in June, 1951. He reported failing vision for several years. Late chronic noncongestive open-angle glaucoma was present in both eyes with vision in the right eye 5/200, unimproved, and in the left eye 20/30 with a greatly constricted visual field in the latter.

After miotics failed to control the intraocular pressure, which was 64 mm. Hg (Schiøtz), cyclodiathermy was performed in July. The complication of slight vitreous bleeding cleared readily.

Three years later, in April, 1954, the intraocular pressure was 34 mm. Hg in the right eye and 30 mm. Hg in the left eye without medication. The vision was about the same in the right eye, but in the left eye it was 20/20 plus, and the visual field was slightly larger than at the time cyclodiathermy was performed.

Case 52

Chronic noncongestive open-angle glaucoma in a white person. K. C., a stenographer, aged 42 years, the sister of a physician, had experienced failing vision over a period of years and had been told that she had glaucoma. On ocular examination in May, 1953, the pupillary reaction was sluggish, and the pupils were partially dilated. There was an open angle with no anterior peripheral synechias visible.

Funduscopic examination revealed a typical glaucomatous disc of the advanced type. A Ronne nasal step and a Bjerrum scotoma were present in both eyes. The facility of outflow was 0.05 in each eye. Corrected vision in both eyes was 20/20.

Ten days after the examination cyclodiathermy was performed on the lower half of both globes. Eight months postoperatively the vision was 20/20 and the intraocular pressure 25.6 mm. Hg (Schiøtz) without medication in both eyes. Two months later, the pressure in both eyes was 16.7 mm. Hg.

Case 22

Chronic noncongestive narrow-angle (iris-block) glaucoma. J. A., a white man, aged 71 years, had a history of glaucoma over a period of several years with gradually failing vision. On ocular examination in July, 1950, the anterior chambers were shallow with many peripheral anterior synechias. Corrected vision was 20/30 in both eyes. The intraocular pressure varied between 38 and 54 mm. Hg (Schiøtz) in both eyes with conservative treatment until February, 1952, when it was definitely determined that the visual fields were contracting and the blindspots getting larger.

Cyclodiathermy was performed below in the lower nasal and temporal quadrants of both eyes. The intraocular pressure has been controlled to date in the right eye in spite of slightly progressive lenticular pathologic changes. In the left eye the pressure ranged as high as 50 mm. Hg until cyclodiathermy was performed in the upper nasal and temporal quadrants in March, 1953. At the last recording in February, 1954, the pressure in this eye was 29.2 mm. Hg without medication. In the right

TABLE 1

SUMMARY OF 80 CASES IN WHICH CYCLODIATHERMY WAS PERFORMED FOR VARIOUS TYPES OF GLAUCOMA*

Name Age Race	Diagnosis	Previous Surgery	Preoperative Tension and Vision	Date of Operation	Cyclodiathermy	Follow-Up	Result
1. B. V. 66 N	Late chronic narrow-angle iris-block glaucoma	Bilateral iridencleisis with corneosclerectomy 4/20/48. Cyclodialysis O.D. Cataract extraction O.D. 1/25/49	O.D. blind; O.S. finger perception 3 ft.	5/ 3/49	O.U. 20 punctures lower halves, 4 mm. from limbus	1 yr.	Tension O.D. 34, O.S. 16. Finger perception O.S. without medication
2. A. K. 42 W	Secondary glaucoma uveitic type, painful eye	Retinal detachment surgery 1927. Supraorbital block O.D. 1949	Tension 70. Blind eye	10/26/49	O.D. lower temporal quadrant 15 punctures 4 mm. from limbus or less	2 yr.	Tension O.D. 40 in 1951; globe not painful
3. C. R. 53, W	O.D. aphakic. Secondary glaucoma	Cataract extraction and discission	Tension 63. Vision O.D. finger perception	11/ 1/49	O.D. 28 punctures temporal half 4–6 mm. from limbus	2 yr.	Tension 33. Corneal scarring. Only light perception
4. A. F. 55, N	Secondary glaucoma. Aphakia	Cataract extraction and cyclodialysis 1949	Tension off scale, hard. Bare light perception	11/ 8/49	O.S. 20 punctures lower half inside 4 mm. from limbus	1 yr.	Tension 43, without medication. Bare light perception
5. F. D. 60 N	Narrow-angle iris-block glaucoma	Bilateral iridectomy and corneosclerectomy 7/21/49	Vision O.D. 20/40, 1949 prior to any surgery; O.S. blind. Tension O.D. 54, O.S. 70	11/29/49 12/27/50	O.D. 18 and O.S. 17 punctures 4 mm. from limbus or less; O.U. 18 punctures above 6 mm. from limbus	1½ yr.	Tension not controlled; off scale, hard O.D., O.S. 49, 6 mo. after second operation. No light perception
6. E. E. 70 W	Secondary glaucoma. Aphakia. Keratopathy of bullous type	Cyclodialysis O.D. 8/28/48	Finger perception. Tension O.D. 61	11/29/49	O.D. 27 punctures, 3 quadrants, 2 below and 1 upper temporal 4–6 mm. from limbus	1 yr.	Tension 30. Vision 10/200, RFC O.D.
7. C. R. 53, W	Secondary glaucoma. Aphakia O.D.	Cataract extraction O.D. 1948. Several needlings thereafter	Tension 38. Vision O.D. 10/200 RFC	12/ 2/49	O.D. 28 punctures temporal half 4–6 mm. from limbus	10 mo.	Tension 25. Vision 15/200 RFC
8. H. W. 65 N	Late wide-angle glaucoma	None	Tension O.D. 40, O.S. 42 with miotics. Vision O.D. 20/50, O.S. 20/70	12/ 5/49	O.D. 18 and O.S. 20 punctures 4 mm. from limbus	1 yr.	Tension O.D. 29, O.S. 33 without medication. Vision O.D. 20/60, O.S. 20/50 –
9. R. J. 61 W	Secondary glaucoma O.S. following central vein thrombosis. Painful eye	None	Tension off scale, hard with 10 mg. weight. Vision O.S. finger perception	12/29/49	O.S. 25 punctures within 5 mm. arc below	8 mo.	Tension 45. No light perception. Globe retained and comfortable
10. M. C. 52 N	Wide open-angle glaucoma. O.S. blind. Hypertensive retinopathy	None	Tension O.U. 43. Vision O.D. 20/100, O.S. blind	12/30/49	O.D. 24 and O.S. 16 punctures 4 mm. from limbus or less	2 yr.	Tension 1951 O.U. 30 with Floropryl on retiring. Vision O.D. 20/200 not improved
11. E. W. 31 N	Late wide open-angle glaucoma O.S.	None	Vision O.S. 20/200 not improved. Tension 70	2/25/50	O.S. 18 punctures lower half 4 mm. from limbus	1½ yr.	Vision 20/200+. Tension 34 with Pilocarpine 2% twice daily
12. F. S. 54 W	Narrow-angle iris-block glaucoma O.U.	Peripheral iridectomy O.D., total iridectomy O.S. 1944	Vision O.D. 20/40, O.S. 20/70 RFC. Tension O.D. 61, O.S. 64	3/14/50	O.D. 32 punctures 2–4 mm. from limbus; 31 punctures O.S. 3–4 mm. from limbus	2 yr.	Tension O.D. 43, O.S. 38 without medication. Vision O.D. 20/40, O.S. 20/100 RFC
13. W. H. 58 N	Secondary glaucoma. Aphakia	Cataract extraction and cyclodialysis 1947	Vision O.D. 20/30+ RFC. Tension 63	7/14/50	O.D. 24 punctures lower half 2–4 mm. from limbus	1½ yr.	Tension 30. Vision 10/200 corrected. Eye white and quiet. Considerable corneal scarring
14. E. H. 36 N	Glaucoma secondary uveitis O.D. Marked keratopathy	None	Tension off scale, hard. Light perception at eye	8/ 9/50	O.D. 30 punctures below combined with broad Graefe iridectomy	6 mo.	Tension 30. Vision light perception. Could not visualize separated retina, probably present preoperatively

* The Schiøtz tonometer was employed throughout. The visual acuity is expressed in corrected vision (RFC) when correction improved the vision.

TABLE 1—(*Continued*)

	Name Age Race	Diagnosis	Previous Surgery	Preoperative Tension and Vision	Date of Operation	Cyclodiathermy	Follow-Up	Result
15.	A. J. 36 N	Late glaucoma. Aphakia O.S. Old residuals of uveitis	Dynamite explosion in childhood. Cataract extraction, multiple discissions	Tension O.S. 49. Vision O.S. 20/100 RFC	2/14/51	O.S. 22 punctures below 4–6 mm. from limbus	2 yr.	Tension O.S. 22. Vision O.S. 20/50 RFC
16.	W. H. 57 W	Aphakic secondary glaucoma	Cataract extraction, cyclodialysis and discission 1947	Vision 20/200 RFC. Tension 70	2/23/51	O.S. 20 punctures 4–6 mm. from limbus, withdrawal of aqueous and air injection into anterior chamber	3 yr.	Tension 26, 1954. Vision 10/200 RFC. Severe pseudomonas keratopathy with resultant corneal scarring
17.	C. B. 52 W	O.S. absolute glaucoma. Practically blind	O.D. enucleated 1 yr. previously. Had been advised to have O.S. removed	Light perception. Tension off scale, hard	2/28/51	O.S. 23 punctures 4 to 6 mm. from limbus below. Air injection into chamber	10 mo.	Hyphema and mild uveitis postoperatively. After 10 mo. tension O.S. 39 without medication. Globe preserved. Light perception
18.	E. Q. 17 W	Secondary glaucoma O.D. Aphakia. Retinal detachment	Cataract extraction. Retinal detachment surgery 1950	Questionable light perception. Tension off scale, hard with 10 mg. weight	6/5/51	O.D. 24 penetrating punctures 4–6 mm. from limbus lower half	4 mo.	Light perception. Tension 22 without medication. Eye white and quiet
19.	R. J. 30 N	Chronic wide open-angle glaucoma O.U.	None	Vision O.D. light perception temporal field; vision O.S. 20/30. Tension O.D. 70, O.S. 30	7/2/51	O.D. 30 and O.S. 28 punctures 4–6 mm. from limbus	3 yr.	Vision O.D. light perception, O.S. 20/20. Tension O.D. 34, O.S. 30 without medication
20.	W. B. 23 N	Secondary glaucoma O.D. following corneal transplantation	Corneal transplant 1949	Vision O.D. finger perception. Tension 43 with active medication	7/13/51	O.D. 30 punctures 4 mm. from limbus or less	1½ yr.	Finger perception. Tension 43 without medication. Another cyclodiathermy and transplant later advised in 1952
21.	J. W. 59 W	Late wide-angle glaucoma	None	Vision O.D. 20/200, O.S. 20/30. Tension O.U. 48	12/10/51	O.D. 14 punctures and 16 O.S. 6 mm. from limbus	2 yr.	Tension O.D. 29, O.S. 25 without medication. Vision O.D. 20/100 −, O.S. 20/20 −
22.	J. A. 71 W	Chronic narrow-angle iris-block glaucoma	None	Tension O.U. 38–54. Vision O.U. 20/30 RFC; fields contracting	2/8/52 3/20/53	O.U. 10 punctures below 4–6 mm. from limbus. 1 yr. later tension O.D. 29, O.S. 48. Cyclodiathermy O.S. above 30 punctures 6–9 mm. from limbus	3 yr.	1½ yr. after second cyclodiathermy vision O.U. 20/30 RFC. Tension O.D. 33, O.S. 29 without medication
23.	C. P. 68 W	Secondary glaucoma. Aphakia	Preliminary iridectomy 1950. Cataract extraction 1951	Tension O.D. 70. Vision finger perception temporal field	3/3/52 2/7/53	O.D. 18 punctures lower half 4–6 mm. from limbus; 30 punctures upper half of globe 6–9 mm. from limbus	2 yr.	Tension 1 yr. after first cyclodiathermy 58; 1 yr. after second cyclodiathermy 37. Major keratopathy associated with herpes zoster 6 mo. after second operation. Vision light perception
24.	J. C. 74 W	Wide open-angle glaucoma. Considerable pigment over trabeculas	None	Tension O.D. 40, O.S. 43. Vision O.D. 20/20, O.S. 20/30 RFC	3/11/52	O.D. 9 and O.S. 10 penetrating punctures below 6 mm. from limbus	1 yr.	Tension O.U. 29 with 2% Pilocarpine at night. Vision O.D. 20/20+, O.S. 20/200. Partial thrombosis central vein O.S. 4 mo. after cyclodiathermy
25.	P. W. 52 N	Late secondary glaucoma. Uveitis O.D.	Total iridectomy with Cortone irrigation of chamber 1/22/52	Vision O.D. 20/50. Tension 61	3/27/52	O.D. 13 punctures lower half 6 mm. from limbus	5 mo.	Tension O.D. 34 without medication. Vision O.D. 20/30
26.	J. A. 1½ W	Secondary glaucoma associated with prematurity. Retrolental fibroplasia	None	Tension O.D. off scale, hard	4/1/52 7/5/52	O.D. 40 punctures lower half; 3 mo. later 40 upper half 6–8 mm. from limbus	2 yr.	Tension O.D. 42 with child straining, but apparently much more comfortable

TABLE 1—(*Continued*)

Name Age Race	Diagnosis	Previous Surgery	Preoperative Tension and Vision	Date of Operation	Cyclodiathermy	Follow-Up	Result
27. W. P. 83 W	O.U. narrow-angle iris-block glaucoma with central vein thrombosis O.S.	None	O.D. blind 5 yr., O.S. light perception temporal field. Tension O.D. 43, O.S. 61	5/ 1/52	O.D. 20 and O.S. 24 punctures 6 mm. from limbus	6 mo.	Tension O.D. 30, O.S. 42 with miotic therapy. Hyphemia O.S. postoperatively with resultant posterior synechias. Eye white and quiet. Light perception
28. H. H. 63 W	Compensated late wide open-angle glaucoma O.S.	None	Tension O.D. 40, O.S. 49. Vision O.D. 20/30+, O.S. 4/200	5/16/52	O.D. 14 and O.S. 15 punctures lower half 4–6 mm. from limbus	2½ yr.	Tension O.U. 29 without medication. Vision O.D. 20/20−, O.S. 5/200+
29. R. D. 70 W	Late chronic narrow-angle iris-block glaucoma almost a bombé O.D. Phthisis bulbi O.S.	None	Tension O.D. 49. Vision 20/20 RFC	6/ 1/52	O.D. 20 punctures below 6–8 mm. from limbus	2 yr.	Tension O.D. 29 with 2% Pilocarpine twice a day. Floropryl on retiring. Vision 20/30 RFC. Original contracting field holding up well
30. J. Z. 42 W	Secondary glaucoma. Thrombosis central retinal vein complicated by retinal separation	None	Vision light perception temporal field. Tension 61	7/ 2/52 11/ 6/52 5/ 8/54	O.S. cyclodiathermy and retinal detachment surgery, 32 nonpenetrating punctures and 30 penetrating applications below. O.S. cyclodiathermy above 25 punctures. Combined cataract extraction O.S.	2 yr.	Tension O.S. 45 with medication after cyclodiathermies. Light perception. Marked lens opacity. Five months after cataract extraction tension O.S. 22. Light perception
31. R. P. 57 N	Late narrow-angle iris block glaucoma O.D. Secondary cataract O.S.	None	Tension O.D. 61, O.S. 26. Vision O.D. no light perception, O.S. light perception and projection, good color perception	7/ 8/52	O.D. 20 punctures lower half 4–6 mm. from limbus; O.S. combined cataract extraction	2 yr.	Vision O.D. no light perception, O.S. 20/50 RFC despite old central area of choroiditis. Tension O.D. 62, O.S. 22
32. J. H. 62 W	Late narrow-angle iris block congestive glaucoma. Bullous keratitis	None	Tension off scale, hard. Light perception at eye	7/15/52	O.D. 24 punctures lower half 4–6 mm. from limbus	6 mo.	Uveokeratitis, hypotony. Whole process subsided with retained globe
33. C. H. 52 N	Late wide open-angle glaucoma O.U.	None	Tension O.U. 43 with glaucomatous therapy. Vision O.D. 20/50, O.S. 20/40 RFC	8/26/52	O.D. 22 punctures, 24 O.S. 4–6 mm. from limbus	1½ yr.	Tension O.U. 33 without medication. Vision O.U. 20/50
34. M. P. 67 N	Very late wide open-angle glaucoma	None	Tension O.D. 52, O.S. 45. Vision O.D. barely light perception, O.S. finger perception	9/18/52	O.D. 23 punctures 26 O.S. 4–6 mm. from limbus	1 yr.	Tension O.D. 33, O.S. 29 without medication. Vision O.U. 15/200
35. A. B. 42 N	Late wide open-angle glaucoma	None	Tension O.D. 48, O.S. 62. Vision O.D. finger perception temporal field, O.S. 20/30 RFC	11/18/52 5/ 5/54	O.U. 40 punctures lower halves 4–6 mm. from limbus; O.U. 50 punctures upper halves 6–10 mm. from limbus	1½ yr.	Tension O.D. 16, O.S. 26 1 mo. after second operation. Vision O.U. 20/100 RFC
36. E. R. 57 W	Aphakia. Glaucoma. Partial thrombosis of central vein. Diabetes	Cataract extraction	Tension 38–45 with active miotics. Vision 20/40 RFC	12/ 1/52 3/ 9/53	O.D. 40 punctures lower half 6–8 mm. from limbus; 3 mo. later, 40 punctures upper half 6–9 mm. from limbus. Cyclodialysis, 1 yr. later	1½ yr.	Tension up to 48 with miotics after second cyclodiathermy; controlled apparently after cyclodialysis. 22 O.S. 4 mo. postoperatively without medication. Vision 20/40 RFC
37. H. L. 75 W	Open wide-angle glaucoma O.U.	None	Tension O.U. 39; with mydriasis 48 O.U. Vision O.D. 20/50, O.S. 20/20 RFC	12/ 5/52	O.U. 40 punctures lower halves 6–9 mm. from limbus	1½ yr.	Tension O.U. 29 with 2% Pilocarpine on retiring. Vision O.D. 20/100, O.S. 20/20 RFC

TABLE 1—(*Continued*)

	Name Age Race	Diagnosis	Previous Surgery	Preoperative Tension and Vision	Date of Operation	Cyclodiathermy	Follow-Up	Result
38.	B, P. 58 W	Narrow-angle iris-block glaucoma	None	Tension O.U. 40–60 with profound miosis. Vision O.D. 20/25–2, O.S. 20/50–1	12/ 5/52	O.U. 40 punctures lower halves 6–8 mm. from limbus	1½ yr.	Tension O.D. 62, O.S. 72. 3 mos. after iris inclusion (1954) vision O.D. 20/50, O.S. 20/40. Tension 18–20
39.	I. F. 59 W	Narrow-angle iris-block glaucoma O.U.	Iridectomy and cataract extraction O.D. 1952	O.D. (aphakic). Tension 62. Vision 20/20 – RFC	12/ 5/52	O.D. 18 punctures below 4–6 mm. from limbus	1½ yr.	Tension O.D. 37 with Prostigmin, Pilocarpine, and Floropryl. Vision 20/20 – RFC
40.	M. McC. 76 W	Surgical anophthalmos O.D. resulting after much surgery for cataract and glaucoma. O.S. secondary glaucoma, aphakia	Cataract extraction 1951. Cyclodialysis and needling 1952. Cyclodialysis and discission late 1952	Tension up to 72 prior to cyclodiathermy. Finger perception	12/ 8/52	O.S. 40 punctures lower half 6–8 mm. from limbus	2½ wk.	Eye later reported enucleated
41.	C. L. 59 W	Wide open-angle glaucoma	None	Tension O.U. 42 with active medication. Vision O.D. 20/30, O.S. 20/20	12/ 9/52 3/ 9/53	O.U. 40 punctures lower halves 6–8 mm. from limbus; 4 mo. later, 40 punctures upper halves 6–8 mm. from limbus	1½ yr.	Tension O.U. 22 3 mo. after second operation. Vision O.D. 20/30 O.S. 20/20 –
42.	I. G. 63 N	Acute congestive narrow-angle glaucoma O.U.	None	Tension off scale, hard O.U.; after active repeated medication O.U. 62. Vision O.U. light perception at eye	12/23/52 1/23/53 6/12/53	O.U. 50 punctures lower halves 6–10 mm. from limbus combined with paracentesis; O.S. 50 punctures upper half; O.D. 50 punctures above and O.S. 15 punctures each around internal and external recti	2 yr.	Tension 1½ yr. later O.U. 29 with Floropryl at night and Diamox twice daily. Cyclodiathermy repeated 1 mo. after first operation O.S. because tension rose to 42. Light perception increased O.U.
43.	J. B. 67 W	Wide open-angle glaucoma	None	Tension 39 with profound miosis. Vision O.D. 20/50, O.S. 20/50	12/29/52	O.U. 40 punctures 6–8 mm. from limbus lower halves. Slight hyphema, uveitis postoperatively	1½ yr.	Tension 25 O.U. Vision 20/50 O.U. Slight residuals of uveitis anterior surface of lens
44.	U. N. 64 W	Aphakia. Secondary glaucoma	Cataract extraction. Iridotomy 5 mo. later	Tension 48–55. Light perception and projection and color perception	1/ 7/53 6/25/53	O.S. 40 punctures lower half 6–9 mm. from limbus; 40 punctures upper half 6–9 mm. from limbus. Iridotomy with Wheeler knife 8/15/53	1½ yr.	Tension 24 O.S. Barely light perception
45.	M. W. 71 W	Secondary glaucoma following herpes zoster ophthalmicus	None	Tension off scale, hard. Finger perception at eye	2/24/53	O.D. 50 punctures 6–10 mm. from limbus lower half	6 mo.	Tension 37. Finger perception at 5 ft.
46.	P. D. 67 W	Immediate post acute episode congestive glaucoma	None	Tension 48 with active medication. Vision 20/50	3/ 7/53	O.S. 40 punctures lower half 6–9 mm. from limbus. Paracentesis of chamber	4 mo.	Tension 37 with active medication. Vision 20/200. Further surgery in the North
47.	O. P. 58 W	Secondary glaucoma. Aphakia. Secondary cataract	Extracapsular cataract extraction	Tension 62. Vision 20/50 RFC	3/19/53	O.S. cyclodiathermy combined with discission. 50 punctures 8–11 mm. from limbus	3 mo.	Tension 22. Vision 20/40 RFC
48.	O. H. 80 W	Secondary glaucoma O.U. Bilateral aphakia	Cataract extraction O.U. Cyclodialysis O.U. 7/10/50	Tension O.D. 55, O.S. 48 with glaucomatous therapy. Vision O.D. 20/40, O.S. 20/30 – RFC	4/ 9/53	O.U. 50 punctures lower halves 6–8 mm. from limbus	1 yr.	Tension O.D. 37, O.S. 29 without therapy. Vision 20/30 O.D., O.S. 20/20 RFC
49.	K. B. 3 W	Microphthalmos O.U. O.D. secondary glaucoma, corneal edema, no view of grounds. O.S. retinal fold	None	Tension 83. Vision questionable	3/11/53 5/ 5/53	O.D. 40 punctures lower half 6–8 mm. from limbus. Tension 48 2 mo. later; 40 punctures upper halves 6–8 mm. from limbus	8 mo.	Tension O.D. 33 6 mo. after second operation with eserine unguentine twice daily

TABLE 1—(*Continued*)

	Name Age Race	Diagnosis	Previous Surgery	Preoperative Tension and Vision	Date of Operation	Cyclodiathermy	Follow-Up	Result
50.	E. D. 43 N	Old late secondary uveitic glaucoma	None	Tension 65. Vision 20/30 RFC	5/15/53	O.D. 50 punctures 6–10 mm. from limbus	1 yr.	Tension 33 with Florapryl twice a week. Vision 20/50
51.	A. T. 66 N	Very late wide open-angle glaucoma	None	Tension O.D. 42, O.S. 47. Vision O.D. gross form, O.S. finger perception	5/19/53	O.U. 30 punctures lower halves 6–8 mm. from limbus	1 yr.	Tension O.U. 29 without medication. Vision O.U. 2/400
52.	K. C. 42 W	Late wide open-angle glaucoma	None	Tension O.D. 48, O.S. 42. Vision O.U. 20/20 RFC. Very poor facility aqueous outflow	5/22/53	O.U. 55 punctures lower halves 6–10 mm. from limbus	10 mo.	Tension O.U. 16 without medication. Vision O.U. 20/20 RFC
53.	A. W. 64 N	Chronic wide open-angle glaucoma. Intumescent lens opacity O.S.	Iris inclusion O.U. early 1953	Tension O.U. 37 poor filtration. Vision O.D. 20/200, O.S. 2/200	6/1/53	O.U. 20 punctures 6–9 mm. from limbus lower half and intracapsular extraction of cataract O.S.	8 mo.	Tension 29 without medication. Vision O.D. 20/100, O.S. 20/50 RFC
54.	A. A. 63 N	Wide open-angle glaucoma	None	Tension O.D. 37, O.S. 48. Vision O.D. 20/20, O.S. 20/200 RFC	6/5/53	O.U. 40 punctures lower halves 6–8 mm. from limbus	1 yr.	Tension O.D. 29, O.S. 33 without medication. Vision O.D. 20/20, O.S. 20/100 RFC
55.	J. McK. 67 W	Late wide open-angle glaucoma. Mature senile cataract with capsular exfoliation	None	Tension 55. Light perception at eye	8/26/53	O.D. 40 punctures 6–10 mm. from limbus and combined intracapsular cataract extraction	6 mo.	Uneventful course. Tension 22 without medication. Light perception present to greater degree
56.	F. S. 29 N	Late wide open-angle glaucoma	None	Tension O.U. 48. Vision O.D. 20/20, O.S. 20/20− RFC. Diminished facility of aqueous outflow	10/8/53	O.U. 55 punctures lower halves 6–10 mm. from limbus	8 mo.	Tension O.U. 29 with eserine unguentine nightly. Vision O.D. 20/20−, O.S. 20/20
57.	J. L. 65 N	Noncongestive narrow-angle iris-block glaucoma	None	Tension O.D. 37, O.S. 67. O.D. finger perception at eye, O.S. no light perception	10/8/53	O.U. 40 punctures lower halves, 6–10 mm. from limbus	6 mo.	Tension O.U. 42 with Pilocarpine 2% twice daily. O.D. finger perception at eye
58.	K. M. 53 W	Wide open-angle glaucoma O.S. Lenticular pathology with capsular exfoliation	Cataract extraction O.D. June 1953, Cyclodialysis O.D. September 1953	Tension O.S. 62. Vision 20/30 RFC	10/20/53	O.S. 40 punctures lower half 6–9 mm. from limbus	5 mo.	Tension 29 with Florapryl three times a week. Vision 20/30−. Only slight progression of lenticular changes
59.	R. S. 45 W	Late open wide-angle glaucoma	None	Tension O.S. 72. Vision O.S. light perception temporal field, blind O.D.	10/29/53 11/10/53 3/23/54	O.S. 38 punctures lower half 6–9 mm. from limbus; 38 punctures upper half 6–9 mm. from limbus; 12 punctures around each insertion of internal and external recti anteriorly and posteriorly	1½ yr.	Tension 40–50 after first operation; 40–50 2 mo. after second operation; 14 3 mo. after third operation. Light perception temporal field
60.	D. W. 64 N	Uveitic secondary glaucoma	None	Tension O.D. off scale, hard, O.S. 55. Vision O.D. finger perception, O.S. 20/400	11/18/53	O.U. 20 punctures lower halves 6–10 mm. from limbus and a broad total iridectomy	7 mo.	Tension O.D. 26, O.S. 34 Vision O.D. finger perception, O.S. 12/200. Cataract surgery advised
61.	B. S. 69 N	Chronic wide open-angle glaucoma. Marked senile lens changes particularly O.D.	None	Tension O.U. 42. Vision O.D. 5/200, O.S. 20/200 RFC	11/27/53	O.U. 50 punctures lower halves 6–10 mm. from limbus and O.D. combined intracapsular cataract extraction	6 mo.	Tension O.D. 25 and O.S. 29. Vision O.D. 20/50+, O.S. 20/100 RFC
62.	P. B. 48 N	Very late wide open-angle glaucoma	None	Tension off scale, hard O.U. Vision O.D. no light perception temporal field, O.S. light perception	12/15/53	O.U. 60 punctures lower halves 6–10 mm. from limbus	7 mo.	Tension O.D. 37, O.S. 29 with 2% Pilocarpine twice daily. Improved light perception in O.S.

TABLE 1—(*Continued*)

	Name Age Race	Diagnosis	Previous Surgery	Preoperative Tension and Vision	Date of Operation	Cyclodiathermy	Follow-Up	Result
63.	G. L. 76 W	Late narrow-angle iris-block glaucoma	Iridencleisis O.D. October 1953	Tension O.D. 48, O.S. 62 with miotics. Vision O.D. 20/30 RFC. Blind O.S.	12/21/53 3/20/54	O.U. 50 punctures lower halves 6–10 mm. from limbus; 50 punctures O.D. upper half 6–10 mm. from limbus	7 mo.	Tension again 48 O.D. after first cyclodiathermy; 3 mo. after second cyclodiathermy 29 with no local medication. Vision O.D. 20/30, O.S. about same, but eye more comfortable
64.	F. M. 67 W	Wide-angle glaucoma. Peripheral synechias, plateau type iris	None	Tension O.D. 55, O.S. 47. Vision O.U. 20/30 – RFC	12/30/53	O.U. 40 punctures lower halves 6–10 mm. from limbus and broad total iridectomy	6 mo.	Tension O.D. 29, O.S. 19. Vision 20/30 RFC O.U. No progressive contraction of fields
65.	G. T. 78 W	Acute congestive glaucoma O.D.	None	Tension off scale, hard. Vision O.D. finger perception at eye	1/8/54	O.D. 41 punctures lower half 6–10 mm. from limbus and total iridectomy, basilar type	6 mo.	Tension 25 without medication. Hyphema after surgery cleared promptly. Vision O.D. finger perception
66.	C. G. 52 W	Glaucoma. Acute congestive episode associated with rubeosis iridis diabetica	None	Tension 77, Light perception O.S.	1/24/54	O.S. 20 punctures lower half each quadrant 6–10 mm. from limbus and broad iridectomy	2 mo.	Tension 40 with eserine unguentine twice daily. Vision finger perception
67.	J. P. 73 W	Noncongestive late narrow-angle iris-block glaucoma. Marked nuclear posterior subcapsular lens opacities	None	Tension 37 O.D., O.S. 62 with profound miosis. Vision O.D. 20/30 – RFC, O.S. light perception	2/2/54	O.U. 50 punctures lower halves 6–9 mm. from limbus; 3 wk. later, combined intracapsular cataract extraction O.S.	4 mo.	Tension O.D. 16 and O.S. 29. Vision O.D. 20/40 RFC, O.S. finger perception. Central retinopathy
68.	N. McD. 75 N	Chronic open wide-angle glaucoma	None	Tension O.D. 45, O.S. 62. Vision O.D. 20/30 –, O.S. gross form	2/10/54	O.D. 49 punctures and O.S. 55 lower halves 6–10 mm. from limbus	4 mo.	Tension O.D. 16, O.S. 29 without medication. Vision O.D. 20/30 –, O.S. finger perception at eye
69.	O. L. 55 W	Narrow-angle iris-block glaucoma. Referred by Dr. A. deRoetth, who reported partial venous thrombosis O.S. 1945	Cyclodiathermy by Dr. deRoetth 1946	Tension O.U. 62. Vision O.D. 20/40 +, O.S. 20/200	2/27/54	O.U. 50 punctures lower halves 6–10 mm. from limbus	1 mo.	Dr. deRoetth reports tension controlled and visual acuity not deteriorating
70.	C. R. 38 W	Open wide-angle glaucoma O.S. Surgical anophthalmos O.D. Much pigment in angle O.S.	Enucleation O.D. 1 yr. previously for melanoma	Tension 38 with mydriatic, provocative test 72. Vision O.S. 20/30 RFC	2/29/54	O.S. 48 punctures lower half 6–10 mm. from limbus	4 mo.	Tension 25 without medication. Vision O.S. 20/30 RFC
71.	S. H. 7 W	Late chronic wide-angle glaucoma. Congenital glaucoma. Sturge-Weber syndrome, cornea 13 mm. diameter O.D.	None	Tension O.D. 62, O.S. 25. Diminished facility of aqueous outflow O.D. 0.05. Considerable blockage of angle with mesodermal tissue O.D. Vision O.D. 20/100	3/9/54	O.D. 44 punctures lower half 6–9 mm. from limbus	3 mo.	Tension 22 with use of Prostigmin twice daily and massage. Vision O.D. 20/50
72.	E. P. 41 W	Secondary glaucoma in old traumatized aphakic eye	Suturing of corneal laceration early 1951. Cyclodialysis late 1951	Tension 55, January 1954. Vision 20/100 RFC	3/9/54	O.D. 50 punctures lower half 6–10 mm. from limbus	4 mo.	Tension 29–33 with Diamox 250 mg. twice daily. Vision O.D. 20/100 RFC
	J. C. 71 N	Late wide open-angle glaucoma	None	Tension O.U. 48. Vision O.D. 10/200, O.S. 10/100	3/17/54	O.D. 52 punctures and O.S. 50 lower halves 6–10 mm. from limbus	3 mo.	Tension O.U. 19 without medication. Vision O.D. 20/200, O.S. 20/100

TABLE 1—(*Continued*)

Name Age Race	Diagnosis	Previous Surgery	Preoperative Tension and Vision	Date of Operation	Cyclodiathermy	Follow-Up	Result
74. K. F. 66 W	Late wide open-angle glaucoma	None	Tension O.D. 55, O.S. 42. Vision O.D. gross form temporal field, O.S. 20/30 RFC, but very contracted field	4/ 6/54	O.D. 51 punctures and 50 O.S. 6–10 mm. from limbus	4 mo.	Serous iritis O.S. easily controlled with Scheperns' solution (subconjunctival homatropine, Neosynephrine and Novocaine). Tension O.D. 29, O.S. 22 without medication. Vision O.D. gross form temporal field, O.S. 20/40 RFC
75. A. H. 45 N	Late open wide-angle glaucoma. Hypertension. Diabetes	None	Tension O.U. 55. Vision O.D. 20/30 RFC, O.S. no light perception	4/ 9/54 6/ 3/54	O.D. 53 punctures and O.S. 50 lower halves 6–10 mm. from limbus; O.U. 48 punctures upper halves 6–10 mm. from limbus	3 mo.	Tension after 2 mo. 48 O.U. After second operation 25 O.U. Vision O.D. 20/30 RFC
76. J. O. 51 N	Late wide open-angle glaucoma	None	Tension O.U. 51. Vision O.D. no light perception, O.S. 20/40 RFC	4/ 9/54	O.U. 50 punctures lower halves 6–10 mm. from limbus	5 mo.	Tension O.U. 19. Vision O.D. no light perception, O.S. 20/40 RFC
77. A. T. 59 N	Late narrow-angle iris-block glaucoma. Much pigment in angle O.D. Phthisis bulbi O.S.	None	Tension O.D. 45. Vision O.D. 20/70 RFC	4/12/54	O.D. 53 punctures lower half 6–10 mm. from limbus	5 mo.	Tension O.D. 13 without medication. Vision O.D. 20/60 RFC
78. W. H. 65 N	Late wide open-angle glaucoma O.D. Incipient cataract O.S.	None	Tension O.D. 48, O.S. 33. Vision O.D. 20/200, O.S. 20/30	4/20/54	O.D. 46 punctures and O.S. 56 lower halves 6–10 mm. from limbus	5 mo.	Tension O.D. 25, O.S. 29. Vision O.D. 20/200, O.S. 20/30
79. E. G. 41 N	Late narrow-angle iris-block glaucoma. Microphthalmos	None	Tension O.D. off scale, hard, O.S. 62. Vision O.D. finger perception temporal field, O.S. 20/40 RFC	5/19/54	O.U. 50 punctures lower halves 6–9 mm. from limbus	4 mo.	Tension O.D. 22, O.S. 16. Vision unaltered
80. J. G. 46 W	Late narrow-angle iris-block glaucoma. Microphthalmos	None	Tension O.D. 55, O.S. 62. Vision O.D. 20/20 –, O.S. 20/20 RFC	5/19/54	O.U. 30 punctures lower halves 6–10 mm. from limbus and peripheral iridectomy	4 mo.	Tension O.D. 29, O.S. 16 with massage of O.D. and Diamox 250 mg. twice daily. Vision O.U. 20/30 RFC

TABLE 2

RESULTS OF CYCLODIATHERMY IN VARIOUS TYPES OF GLAUCOMA (120 EYES)

	Number	Percent
Tension (30 mm. Hg Schiøtz or less)		
Controlled without miotics	64	53.3
Controlled with miotics	19	15.8
Hypotonic	1	0.8
Tension reduced 20 to 40 mm. Hg	22	18.3
Uncontrolled	13	10.8
Enucleated	1	0.8
Eviscerated	0	
TOTAL	120	

TABLE 3

VISUAL RESULTS OF CYCLODIATHERMY IN VARIOUS TYPES OF GLAUCOMA (120 EYES)

	Number	Percent
Vision improved	40	33.3
Vision unchanged	54	45.0
Vision decreased	22	18.3
Vision lost	4	3.3
TOTAL	120	

eye, with the use of Carcholin alone twice a day the pressure was 33.1 mm. Hg. The corrected vision was 20/30 in both eyes.

CASE 61*

Cyclodiathermy combined with cataract extraction. B. S., a Negress, aged 69 years, had experienced loss of vision over a period of 10 years, with a diagnosis of glaucoma. Ocular examination in September, 1952, disclosed glaucoma of the open-angle type, pronounced nuclear opacities of the lens, and restricted visual fields. In both eyes considerable excavation of the disc and displacement of the vessel funnels were present. Vision in the right eye was 5/200, unimproved, and in the left eye 20/200, unimproved. The intraocular pressure with profound miosis was 42.5 mm. Hg (Schiøtz).

At operation one week following the examination, cyclodiathermy was performed on the lower half of both globes, and at the same time a combined intracapsular cataract extraction was performed in the right eye. The postoperative course was uneventful. Five months after the operation vision in both eyes with refraction corrected was 20/100; the intraocular pressure was 25.6 and 29.2 mm. Hg in the right and left eyes, respectively. Cataract extraction is planned for the left eye in the immediate future. This case was demonstrated at the 1954 meeting of the Florida Society of Ophthalmology and Otolaryngology.

CASE 67

Late chronic noncongestive narrow-angle (iris-block) glaucoma associated with lenticular pathologic changes. J. P., a physician's wife, aged 73 years, gave a history in December, 1953, of gradual loss of vision, particularly in the left eye. She was using a two-percent solution of pilocarpine three times daily in both eyes and a four-percent solution four times a day in the left eye. The corrected vision in the right eye was 20/30, minus, and in the left eye 10/200, unimproved. Under profound miosis the intraocular pressure was 25.6 mm. Hg (Schiøtz) in the right eye and 62.9 mm. Hg in the left eye. In both eyes the glaucomatous changes in the disc and the nuclear anterior and posterior subcapsular changes in the lens were pronounced.

In January, 1954, cyclodiathermy was performed on the lower half of the globe in both eyes, and in February combined intracapsular extraction of the lens was performed in the left eye under local

* The patient in Case 61 was seen in the fall of 1955. The cataract extraction had been done on the left eye in December, 1954. At the time of the last examination the corrected distance vision was 20/40— in the right eye and 20/100 in the left eye. The intraocular pressure was 23.4 mm. Hg (Schiøtz) in the right eye and 27.1 mm. Hg in the left eye.

TABLE 4

COMPARISON OF RESULTS IN WHITE AND NEGRO PATIENTS

	White 65 Eyes (47 Cases)		Negro 55 Eyes (33 Cases)	
	Number	Percent	Number	Percent
Tension 30 mm. Hg (Schiøtz) or less				
Controlled without miotics	35	53.8	29	52.7
Controlled with miotics	11	16.9	8	14.5
Tension reduced 20 to 40 mm. Hg	12	18.4	10	18.1
Uncontrolled	6	9.2	7	12.7
Vision improved	17	26.1	23	41.8
Vision unchanged	27	41.5	27	49.0
Vision decreased	15	23.0	7	12.7
Vision lost	3	4.6	1	1.8

TABLE 5

POSTOPERATIVE COMPLICATIONS FOLLOWING CYCLODIATHERMY (120 EYES)

Complications	Number	Percent
Immediate		
Hyphema	3	2.5
Uveitis	2	1.6
Delayed		
Pseudomonas keratopathy	1	0.8
Partial thrombosis of central vein	1	0.8
Glaucoma (absolute)	1	0.8

anesthesia, as the intraocular pressure was normalized in both eyes following the cyclodiathermy. The pressure remains stabilized, being 16.7 mm. Hg in the right eye and 29.2 mm. Hg in the left eye early in April, 1954. The vision was 20/40 in the right eye and finger perception in the left eye.

CASE 66

Cyclodiathermy in the treatment of glaucoma secondary to rubeosis iridis diabetica. C. G., a white man, aged 52 years, was referred by Dr. M. A. O'Toole of Clinton, Massachusetts, in January, 1954. There was a history of diabetes with many severe acute episodes of rubeosis iridis diabetica glaucoma in the left eye. He had been using a four-percent solution of pilocarpine in both eyes eight times daily. On ocular examination, with maximum miosis signs of chronic noncongestive narrow-angle (iris-block) glaucoma were observed in the right eye. In the left eye a pronounced congestive phase was present. The intraocular pressure was 77.3 mm. Hg (Schiøtz). Corneal edema was also pronounced, as was vasculogenesis of the iris with tremendous vessels. The pupil was dilated and fixed. The intraocular pressure was not controlled with the most energetic conservative treatment.

Under local anesthesia cyclodiathermy was performed in this eye on the lower half of the globe in the nasal and temporal quadrants, several vitreous presentations through the punctures softening the eye. After closure of the conjunctiva, a classical Graefe iridectomy was performed from above with no complications. The postoperative course was uneventful except for a rather persistent hyphema, which gradually cleared within two weeks. The diabetes was not well controlled during the postoperative period, but six weeks after these surgical measures the intraocular pressure was down to 40 mm. Hg with the use of eserine ointment in the eye twice a day and Rutorbin and CVP by mouth. Surprisingly, considerable visual function remained in this eye.

TABLE 6

CYCLODIATHERMY COMBINED WITH OTHER PROCEDURES (120 EYES)

Procedure	Number	Percent
Total iridectomy	7	8.7
Peripheral iridectomy	2	1.6
Paracentesis and air injection	5	4.1
Retinal detachment surgery	1	0.8
Combined cataract extraction	5	4.1
Discission	1	0.8

Certainly, I would not leave the impression that all cyclodiathermy leads to the Elysian fields in the treatment of glaucoma. It is by no means a panacea, as the two cases which will now be described will show. They afford examples of the unsuccessful employment of this therapy in chronic noncongestive narrow-angle (iris-block) glaucoma and in the aphakic eye.

CASE 38

Chronic noncongestive narrow-angle (iris-block) glaucoma. B. P., a white woman, aged 58 years, was referred by Dr. Albert C. Esposito of Huntington, West Virginia. There was a history of failing vision over a period of several years with treatment by Dr. Esposito for the preceding three months. His report, in which I concurred, was: Shallow anterior chambers, pronounced cupping of the discs, vision in the right eye 20/25 — 2 and in the left eye 20/50 — 1, and intraocular pressure varying between 40 and 60 mm. Hg (Schiøtz) in both eyes. With the administration of a four-percent solution of pilocarpine in each eye every three hours during the day and once during the night the pressure was normalized most of the time. There was in both eyes constriction of the visual fields with loss of the nasal field in the left eye.

After a considerable period of observation, the patient was subjected to cyclodiathermy in both eyes in December, 1952. The pressure then was controlled fairly well until April, 1953. Thereafter, despite the use of miotics it was elevated at times, particularly in the left eye. Although vision was holding up well, the visual fields were becoming constricted in the right eye. On March 2, 1954, iridencleisis was performed in both eyes with inclusion of both iris pillars under local anesthesia. To date, the pressure has been completely normalized, the range being 18 to 20 mm. Hg without medication.

CASE 58

Cyclodiathermy in aphakia. K. M., a white woman, aged 53 years, underwent combined intracapsular cataract extraction in the left eye in June, 1953, with no complications. Corrected vision two months later was 20/30, but four months after the operation the intraocular pressure was elevated to as high as 62.9 mm. Hg (Schiøtz). Cyclodiathermy was performed on the lower half of the globe with control of the pressure for an-

other three months. It then became elevated again and this time conventional cyclodialysis was performed with an air injection into the anterior chamber. The pressure has remained under control, and the corrected vision in this eye is 20/30 plus.

The eye in this case was one of 14 eyes in this series in which glaucoma was associated with aphakia. In only three of the 14 eyes was cyclodiathermy unsuccessful.

Discussion

Obviously, this study is limited in scope by numerous factors. It is offered to suggest that:

1. Cyclodiathermy is a safe and also frequently an effectual procedure which is not fraught with many unusual complications, perhaps no more than the older procedures.

2. It may be performed as a preliminary procedure or simultaneously with a cataract extraction in indicated cases.

3. It is an operation which does not mutilate or distort the ordinary pathways of an extraction, thus posing no difficulties should cataract surgery later become necessary.

4. The procedure may be repeated with safety at proper intervals twice or even three times in different areas.

5. It requires the minimal period of hospitalization. The newer technique of placing the diathermic applications a greater distance from the limbus and in refractory cases approaching the long ciliary vessels and nerves along the recti muscles has brought improved results. Also, with the advent of vitreous presentation one feels much safer in avoiding any acute episode of glaucoma.

In my opinion, this operation is not an office procedure, as described by Hurwitz,[19] despite current advertisements that leading ophthalmologists are employing it that way. On the other hand, there is the consideration that Diamox, or some similar future product, may make this and other operative procedures for glaucoma unnecessary. This new agent, described as in effect a medical cyclodiathermy both controllable and reversible, appears to give promise of reducing intraocular pressure to a level where ordinary surgery, such as cataract extraction, may be performed satisfactorily and with no more danger than in the common procedures in the eye with normal pressure. Time alone will determine whether or not this therapy, which reduces the facility of aqueous inflow, will have great bearing on the indications for glaucoma surgery.

The modus operandi of lowering intraocular pressure by cyclodiathermy has not yet been adequately explained. Some authors adhere to the belief that the procedure diminishes the production of aqueous humor either by atrophy of the uveal tract at the site of application of the electrode and also anteriorly and posteriorly, or by changes in the nerve pathways leading to the ciliary body which cause a change in the neuroregulatory mechanism. Personal discussion with a number of ophthalmic surgeons has seemed to indicate the consensus among them that cyclodialysis likewise may act on the neuroregulatory system in a similar way rather than by forming a communication between the anterior chamber and the suprachoroidal space.

Whatever the mechanism of action, cyclodiathermy appears to be winning its place in ophthalmic surgery. The different authors have made various uses of it. While Vogt[4] used it in a number of cases in preparation for cataract surgery, Sugar,[20] on the other hand, found use for the procedure only "in blind painful glaucomatous eyes where enucleation is psychologically premature." Blake,[21] however, recently employed it in the treatment of glaucoma complicating congenital aniridia, a most difficult problem, and after wide inquiry among ophthalmologists he concluded that this operation is becoming increasingly popular and modifications in techniques are making for better results.

It is my belief, contrary to that of many ophthalmologists, that the danger of postoperative complications, particularly phthisis bulbi, has been greatly magnified. My observation of the small series presented leads me to conclude that there are probably no

more complications with cyclodiathermy than with standard glaucoma procedures, particularly since the new technique has been employed. The main complication of the operation has been a serous nongranulomatous type of iritis easily controllable with therapy. It is my impression that in my cases the operation has not precipitated nor caused unusual progression of lenticular pathologic changes, as occasionally happens in iris inclusion and trephining procedures. Berens, Sheppard, and Duel[22] found cyclodiathermy a useful procedure and observed in 1950: "The most dread postoperative complication is sympathetic ophthalmia. So far, in the total of 766 cyclodiathermy operations and 108 cycloelectrolysis operations reported in the United States of America, no unquestioned case of sympathetic ophthalmitis has followed either procedure." This complication did not occur in my series.

At the time cyclodiathermy was beginning to regain favor, Arruga[10] stated that performing the punctures too near the limbus had made corneal opacities the complication most frequently encountered. He mentioned opacity of the lens, iridocyclitis, and hemorrhage into the anterior chamber as other complications and pointed out that loss of vitreous, which is not a complication, must even be provoked to a certain extent. Adding that recurrence of the hypertension constitutes failure of the operation, he observed that "this does not occur as frequently as the poor quality of the eyes operated by cyclodiathermy would lead one to expect, since the results are rather promising."

Cowan,[23] in 1951, summarized the status of perforating cyclodiathermy at that time in these words: "If its long-term effects live up to its early promise, glaucoma surgery may very well be revolutionized in the direction of further simplicity. We have not reached this desired goal yet. The operation has been done in too few cases, by too few operators, and the patients have been followed for too short a time. The skeptics, as well as the enthusiasts, will have to be heard from. However, enough success has been achieved to suggest that a surgical principle of great value has been discovered. Especially significant are the favorable results in some of those conditions which had heretofore been considered intractable, especially rubeosis iridis and absolute glaucoma."

My experience leads me, three years later, to concur in the conclusion of Cowan[23] that a valuable surgical principle not to be underestimated has become available. With him I also agree that the ultimate in technique may not yet have been evolved, but, in his words, "whatever factor is responsible for the success of the cyclodiathermy should, and will, be exploited through many other techniques until its full measure of benefits can be applied."

It is noteworthy that the enthusiasm of Castroviejo[11] for this procedure has not waned. In a personal communication to me on April 12, 1954, he stated: "My views on this operation have not changed. I continue to use it in all kinds of glaucoma and feel that it is superior to any other type of glaucoma surgery."

Conclusion

Basically, it is my conclusion that cyclodiathermy has great potential value in congenital glaucoma, open-angle glaucoma, narrow-angle (iris-block) glaucoma to a lesser degree, glaucoma associated with congenital defects of the globe, and secondary glaucoma of all types. Also, it has special value in combination with operative procedures such as cataract extraction, much as a posterior sclerotomy or an iridectomy has; as a preliminary operation prior to a cataract extraction, it is likewise valuable, and in combination with iridectomy in the treatment of congestive glaucoma it gives one the advantage of performing the iridectomy on a soft globe. In 11 of 14 aphakic eyes the procedure has been successful in my hands, the intraocular pressure in the remaining three being normalized later by cyclodialysis.

It is noteworthy that in the past, opera-

tions for glaucoma were designed to eliminate the aqueous. Now, the newer methods in cyclodiathermy and cycloelectrolysis aim to decrease the production of aqueous. The newer technique in cyclodiathermy has brought improved results, and the simplicity of the operation is in its favor. The ideal surgical approach, as pointed out recently by Weekers,[24] would be an operative procedure or combined procedures which would affect favorably the rate of aqueous production and also the facility of aqueous outflow. This paper is presented in the hope of stimulating the development of such a solution to the problem of glaucoma surgery.

A series of 80 cases is reported and analyzed in which cyclodiathermy was employed in the treatment of various types of glaucoma with gratifying results. The cases are summarized in Table 1, and the results in Tables 2 to 6. Six cases in which this therapy was successfully employed and two in which it was a failure are described. The old and the new techniques are discussed, and the role of the procedure in glaucoma surgery is evaluated.

In evaluating the results of any surgical treatment of glaucoma, one must keep in mind the broad range of results which may be termed successful. In many instances patients seek treatment only after the glaucoma is far advanced and some are blind in one eye. Recently, Lloyd[25] aptly observed: "If the tension can be controlled or an enucleation avoided, that is surely as satisfactory a result as reducing the tension, enlarging the field, and improving the vision in eyes with vision such as 20/30. The important consideration is that the standard for success in glaucoma is control of tension and retention of vision in some cases, but in others control of tension is just as much a triumph, and in still other cases avoiding an enucleation, even with higher than normal tension, if the eye is not troublesome, is a greater accomplishment." Each individual case has its own yardstick of success.

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Addendum

Since this paper was submitted for publication, cyclodiathermy has been performed on 38 eyes with even more favorable results than indicated in the series reported herein. I have been particularly impressed with the efficacy of cyclodiathermy in wide-angle glaucoma in the Negro. From the results in these additional cases and a further evaluation of the results in the cases reported, it is my impression that this type of procedure fulfils the need in one of the most difficult types of glaucoma, the open-angle type in the Negro.

References

1. Weve, H. J. M.: Clinische Lessen, Nederl. tijdschr. v. geneesk., **76**:5335, 1932.

2. Albaugh, C. H., and Dunphy, E. B.: Cyclodiathermy: An operation for the treatment of glaucoma. Arch. Ophth., **27**:543-557 (Mar.) 1942.

3. Weekers, L.: Mode d'action des operations antiglaucomateuses. Ophthalmologica, **118**:564-574 (Oct.-Nov.) 1949.

4. Vogt, A.: Versuche zur intraocularen Druckherabsetzung mittelst Diathermieschädigung des Corpus ciliare (Zyklodiathermiestichelung). Schweiz. med. Wchnschr., **66**:593 (June) 1936; Ergebnisse der Diathermiestichelung des Corpus ciliare (Zyklodiathermiestichelung) gegen Glaukom. Klin. Monatsbl. f. Augenh., **99**:9-15 (July) 1937; Die Zyklodiathermiepunktur (Z.D.P.) gegen Glaukom. Ibid., **103**:591-599 (Dec.) 1939; and Cyclodiathermy puncture in cases of glaucoma. Brit. J. Ophth., **24**:288-297 (June) 1940.

5. Scheie, H. G.: Glaucoma: A review of the literature 1951-1952. Arch. Ophth., **48**:752-782 (Dec.) 1952.

6. Reiser, K. A.: Die "Skleraldiathermiepunktur" (S.D.P.), eine einfache Glaukomoperation. Klin. Monatsbl. f. Augenh., **115**:491-500, 1949. Also: Bericht über die Operationsergebnisse mit der Skleraldiathermiepunktur (S.D.P.) Ber. deutsch. ophth. Gesellsch., **56**:155-158, 1951.

7. Biozzi, G.: Sulla coagulazione dell'arteria ciliare posteriore lunga (reperto oftalmoscopico). Gior. ital. oftal., **2**:380-383 (Sept.-Oct.) 1949.

8. Arató, I.: La angiodiatermia y su aplicacion en el glaucoma, Arch. Soc. oftal. hispano-am., **9**:746-758 (July) 1949.

9. Arruga, H.: La diatermia ciliar en el tratamiento del glaucoma. Arch. Soc. oftal. hispano-am., **10**:224-229 (Mar.) 1950.

10. ———: Ocular Surgery. New York, McGraw-Hill, Inc., 1952, ed. 3, pp. 718-723.
11. Castroviejo, R.: Lecture, University of Florida Midwinter Seminar in Ophthalmology and Otolaryngology, Miami Beach, Florida, January 18-23, 1952. Letter dated April 12, 1954.
12. Haas, J. S.: Glaucoma: A review of the literature for 1952-1953. Arch. Ophth., **50**:764-778 (Dec.) 1953.
13. Neubauer, H.: Die nichtperforierende Zyklodiathermie dach Grüter. Klin. Monatsbl. f. Augenh., **121**:9-15 (Jan.) 1952.
14. Arató, S.: Results of angiodiathermy on the basis of 100 operations. Ophthalmologica, **125**:117-124 (Feb.) 1953.
15. Scheie, H. G.: Cyclodiathermy in the treatment of glaucoma. West. J. Surg., **60**:322-326 (July) 1952.
16. Lachman, B. E., and Rockwell, P. A.: Follow-up study of 39 patients with glaucoma treated with cyclodiathermy. Arch. Ophth., **50**:265-266 (Aug.) 1953.
17. Forbes, S. B.: Buphthalmos: Results from operative procedures particularly cyclodiathermy: Report of six cases. Am. J. Ophth., **35**:393-398 (Mar.) 1952.
18. deRoetth, A.: Cyclodiathermy in treatment of glaucoma due to rubeosis iridis diabetica. Arch. Ophth., **35**:20-22 (Jan.) 1946.
19. Hurwitz, P.: Electrosurgical treatment of glaucoma as an office procedure: Preliminary report. E.E.N.T. Month., **32**:380-383 (July) 1953.
20. Sugar, H. S.: The Glaucomas. St. Louis, Mosby, 1951, pp. 419-424.
21. Blake, E. M.: The surgical treatment of glaucoma complicating congenital aniridia. Am. J. Ophth., **36**:907-909 (July) 1953.
22. Berens, C., Sheppard, L. B., and Duel, A. B., Jr.: The surgery of glaucoma: Cycloelectrolysis versus cyclodiathermy: A report of 108 cycloelectrolysis and 766 cyclodiathermy operations. Acta XVI Concilium Ophthalmologicum (Britannia) 1950, pp. 959-970.
23. Cowan, T. H.: In discussion of Rubin, I. E., Romig, J. E., and Molloy, J. H.: Early results of perforating cyclodiathermy in treatment of glaucoma. Arch. Ophth., **47**:544-547 (Apr.) 1952.
24. Personal interview with Dr. R. Weekers of Belgium at the XVII International Congress of Ophthalmology, 1954, New York, September 13-17, 1954.
25. Personal communication from Dr. Ralph I. Lloyd, Brooklyn, New York, dated October 1, 1954.

TREATMENT OF OCULAR HYPERTENSION BY ADRENALIN AND DIVERSE SYMPATHOMIMETIC AMINES*

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Hamburger,[1] in 1923, noted that the instillation of two-percent adrenalin induced a reduction of tension in glaucoma simplex. Goldmann,[2] in 1951, attributed this effect to a prolonged reduction in the rate of aqueous formation.

In recent publications Weekers, Prijot, and Gustin[3, 4] have shown by Grant's technique of tonography that adrenalin lowers the ocular tension in open-angle glaucoma without affecting however the pathologically increased resistance to aqueous flow. This result would seem to be occasioned by a lessened formation of aqueous. As the miotics lower ocular tension by augmenting the facility of flow, adrenalin and miotics play a complementary role. The former reduces the formation of aqueous, the latter facilitates its drainage. The two in association provide a local treatment particularly efficacious for glaucoma simplex (open-angle glaucoma).

The theoretic and practical importance of this tension-reducing action of adrenalin has stimulated further research on the mechanism involved. The present study consists of two parts: (1) The measurement of changes in the delivery of aqueous under the influence of adrenalin; (2) a similar study with diverse sympathomimetic amines.

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I. Modification of Aqueous Production under the Influence of Adrenalin

a. Method of Measurement

Our method, based on that of Langley and MacDonald,[5] measures the speed of the disappearance of fluorescein from the anterior chamber after a previous instillation over the cornea. The fluorometer and the details of procedure have been described by Weekers and Delmarcelle.[6] After fluorescein is dropped in the eye, the concentration of the dye in the anterior chamber increases first, then progressively decreases. At the feeble concentration presented in the anterior chamber the role of diffusion in the elimination of the dye is but slight. The reduction of the concentration of the dye in percentage per minute is calculated by the following formula:

$$C = \frac{2.3 \log. \frac{\text{conc.}t_1}{\text{conc.}t_2}}{t_2 - t_1}$$

Conc.t_1 and Conc.t_2 are respectively the concentrations of fluorescein in the anterior chamber at the beginning and end of a period of decoloration of the aqueous. In normal subjects C varies from 0.33 to 0.65, the average value being 0.48.

This method does not permit the calculation of aqueous flow in cu.mm. per minute as it does not take into account the volume of the anterior chamber. Though less precise than the fluorometric method of Goldmann, its simplicity has facilitated its clinical application in numerous cases (Weekers and Delmarcelle[6]). The information obtained by this fluorometric method on the intraocular current of aqueous is generally in accord with the tonographic calculations of aqueous flow.

b. Results

Fluorometric measurements of flow were made 24 hours after instillation of two-percent *l*-adrenalin on 15 normal subjects, 13 patients with glaucoma simplex (open-angle glaucoma), and three cases of glaucoma following flat chamber after cataract extraction. The data are compared with those of a previous study in which the aqueous flow was measured by the same method in 64 normal subjects, 20 patients with untreated open-angle glaucoma and six untreated cases of glaucoma following flat chamber after cataract extraction. The findings are summarized in Table 1.

The instillation of two-percent *l*evorotatory adrenalin induces a lasting diminution of aqueous production. This conclusion is supported both by direct fluorometric measurements of aqueous flow and by tonographic measurements published previously (Weekers, Prijot, and Gustin[3, 4]).

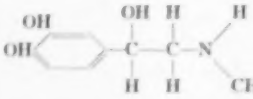
TABLE 1

Reduction of Aqueous Flow under the Influence of One Instillation of Levorotatory Adrenalin

	Without Treatment					24 Hr. after One Instillation of *l*-adrenalin				
	Number of Cases	Average Ocular Tension (mm. Hg)	Coefficient of Flow			Number of Cases	Average Ocular Tension (mm. Hg)	Coefficient of Flow		
			Min.	Mean	Max.			Min.	Mean	Max.
Normal subject	64	16	0.33	*0.48*	0.65	15	13	0.13	*0.34*	0.46
Open-angle glaucoma	20	28	0.30	*0.43*	0.55	13	17	0.28	*0.33*	0.45
Glaucoma of aphakic eye	6	High	0.44	*0.51*	0.60	3	17	0.21	*0.30*	0.40

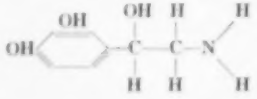
II. The effect on ocular tension of diverse sympathomimetic drugs

We have compared the effects on ocular tension of *l*-adrenalin, *d*-adrenalin, adrenalone, noradrenalin, and aleudrine.* These substances were chosen to facilitate insight into the tension-reducing mechanism. Levorotatory adrenalin, two-percent concentration, is the standard of comparison. It has this structural formula:

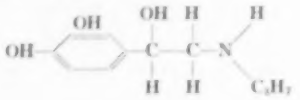


Dextrorotatory adrenalin was used to learn whether the effect on ocular tension was due to sympathetic stimulation or to some other factor, as the sympathomimetic action of *d*-adrenalin is very much less marked than that of *l*-adrenalin. Adrenalone served the same purpose. This substance results from the replacement of hydroxyl in the lateral chain by ketone. Its sympathomimetic activity is extremely feeble.

The utilization of noradrenalin was dictated by other considerations. Ahlquist and Gaddum classify the activities of adrenalin in two groups—alpha and beta. The alpha actions include all motor effects: enhancement of smooth muscle tone, augmentation of secretion, and so forth. The much more specific beta actions are tachycardia in mammals, inhibition of smooth muscle, and the influence on metabolism and the central nervous system. The alpha actions are markedly fortified by cocaine, but not the beta actions. Noradrenalin possesses the alpha actions of adrenalin but very little beta activity. Its structural formula is:



In aleudrine (isopropyl noradrenalin)* the alkyl radical is attached to nitrogen as shown in the formula below. This exaggerates the beta actions of *l*-adrenalin and diminishes the alpha effects (Bacq[7]).



a. Material and conditions of examination

This investigation was concerned almost exclusively with patients affected by open-angle glaucoma. Cases of narrow-angle glaucoma were eliminated by careful gonioscopic examinations since some of the amines used are mydriatic (*l*-adrenalin, noradrenalin) and mydriasis in narrow-angle glaucoma would provoke occlusion of the iridocorneal angle with a resulting increased resistance to aqueous flow and a consequent rise in ocular tension in spite of lessened flow of aqueous.

The tests of each drug were generally continued on the same patient for about two weeks, and the ocular tension was noted two to three times per week. The tests with aleudrine were of shorter duration for reasons explained later. The figures in the appended tables are averages of several tonometric measurements. All measurements were made 18 hours or more after the instillation of the drug in order to register the lasting effect on tension due to modification of aqueous production and not the immediate effect on tension which could be attributed to vasomotor changes. All solutions were instilled in the evening, one drop daily.

The solution of *l*-adrenalin was according to the following prescription:

	(gr.)
l-adrenalin chlorhydrate equivalent to 2-percent *l*-adrenalin base	
Sodium metabisulfite	.03
Chlorobutanol	.03
Sodium chloride	.02
Pontocaine	.05
Desogen (Geigy) (1:50,000)	
Sterile distilled water	10.00

* Translator's note. Isopropyl noradrenalin is marketed in America under the trade names Isuprel (Winthrop-Stearns), Norisodrine (Abbott), and Isonorin (Smith, Carrell, Dunham).

TABLE 2

OCULAR TENSION AS AFFECTED BY *l*-ADRENALIN AND *d*-ADRENALIN

Without Treatment (mm. Hg)	After *l*-adrenalin (mm. Hg)	Without Treatment (mm. Hg)	After *d*-adrenalin (mm. Hg)
25	15	26	23
26	15	26	25
26	20	26	25
27	20	26.5	25.5
27	22	27	27
27	20	27	29
28	20	27	24
34	20	27.5	24
35	16	36	31
36	15	39	35
45	18	44	36
AVERAGE 30.5	18.3	30.2	27.7

The other sympathomimetic amines were prepared in a concentration equimolar to two-percent *l*-adrenalin. When racemic compounds had to be used, as with noradrenalin and aleudrine, the concentrations were doubled as investigation showed that *d*-adrenalin was almost totally ineffective.

b. RESULTS

Table 2 shows that *l*-adrenalin lowers the ocular tension much more than *d*-adrenalin in patients affected with glaucoma simplex (open-angle glaucoma). Occasionally the *d*-adrenalin solution on oxidizing is so altered as to become a mydriatic and acquire tension-reducing power. This occurs inconstantly and was not systematically studied.

TABLE 3

OCULAR TENSION AS AFFECTED BY *l*-ADRENALIN AND ADRENALONE

Without Treatment (mm. Hg)	After *l*-adrenalin (mm. Hg)	After Adrenalone (mm. Hg)	After *l*-adrenalin plus Adrenalone (mm. Hg)
23	20	26	19
24	18	31	20.5
27	22	24.5	21.5
27	24	30	21
28	18	23	18
29	21	32	21
30	19	28	19
30	20	27	18
32	20	30	20
39	23	39	21.5
AVERAGE 28.9	20.5	29.0	19.9

Table 3 demonstrates that *l*-adrenalone is much less active than *l*-adrenalin. A mixture of two-percent *l*-adrenalone and two-percent *l*-adrenalin was no more effective than two-percent *l*-adrenalin alone. The "glaucosan" of Hamburger was such a mixture and in a previous study[3, 4] we employed a similar pharmaceutical preparation. We use now the two-percent *l*-adrenalin prescription previously discussed.

Table 4 shows that racemic noradrenalin lowers ocular tension but less consistently than *l*-adrenalin.

The tests with aleudrine ran into difficulties. Instillation of the aleudrine solution provoked almost immediately a brief though marked tachycardia. For this reason and because the solutions rapidly become inert, the observations with aleudrine were generally of short duration. It is evident, how-

TABLE 4

OCULAR TENSION AS AFFECTED BY *l*-ADRENALIN AND NORADRENALIN

Without treatment (mm. Hg)	After *l*-adrenalin (mm. Hg)	After Noradrenalin (mm. Hg)
24	21	25.5
24.5	21	22.5
25	25	29
25	20	24
25	19.5	20.5
26	19	22
26	19	22
26	19	19
26	18	18
26	21	22
26.5	24	24
27	21.5	29
28	19	20.5
28	—	19
29	21	26
29	24.5	25
30	19	19
30	19	22
30	19	20
31	18	24
32	20	21.5
32	19	22
34	22	35
39	23	36.5
AVERAGE 28.2	20.2	23.7

TABLE 5

OCULAR TENSION AS AFFECTED BY *l*-ADRENALIN AND ALEUDRINE

Without Treatment	After *l*-adrenalin	After Aleudrine
45.5	—	29
45	21	22
39	21.5	24
39	18	20
37	—	22
32	20	26
32	24.5	15
30	19	14
30	20	22
30	19	17
29	25	21
27.5	—	19.5
26	18	20
28	—	20
25	20	21
25	—	19.8
24.5	20	20
24	17.5	17.5
24	17.5	17.5
24	20.5	18
25	17	18
AVERAGE *30.9*	*19.9*	*20.2*

ever, that aleudrine lowers the tension in open-angle glaucoma (table 5). Though aleudrine is neither a mydriatic nor a vasoconstrictor, its action is comparable to that of *l*-adrenalin. In the present study we were unable to quantitatively assess the comparative tension-lowering effect of the two drugs. The graphs (figs. 1 and 2) suggest that, though their effects are approximately of the same order, *l*-adrenalin has an apparently more lasting action than aleudrine.

COMMENT

The tonographic measurements previously published[3, 4] and the fluorometric measurements of flow in the present study definitely establish that the tension-lowering action of *l*-adrenalin in open-angle glaucoma results from a reduction of aqueous formation and not from an improvement of drainage conditions. The comparison of the tension-reducing action of diverse sympathomimetic amines clarifies the mechanism through which *l*-adrenalin inhibits the formation of aqueous. Drugs without appreciable sympathomimetic activity like *d*-adrenalin and adrenalone likewise lack a tension-reducing effect. The reduced tension apparently results then from sympathetic stimulation.

The hypothesis that the reduction of the formation of aqueous is determined by vasoconstriction and the lessened blood flow in the ciliary body that follows should hence be abandoned. The reduction in tension after the instillation of *l*-adrenalin is much more prolonged than the vasoconstriction visible in the conjunctiva; moreover aleudrine, which is not a vasoconstrictor, possesses like *l*-adrenalin the same property of lowering ocular tension. A plausible hypothesis according to which *l*-adrenalin and aleudrine alter the metabolic processes required for the formation of aqueous is proposed.

This concept is of practical clinical importance. In many cases of ocular hypertension the obstacle to the drainage of aqueous is so extensive that miotics cannot ameliorate drainage nor consequently reduce ocular tension. In this contingency an adjuvant that reduces the formation of aqueous may retard the necessity of surgical intervention.

Various therapeutic measures recently proposed reduce the formation of aqueous, such as retrociliary diathermy, Diamox, and some sympathomimetic amines. Each of these therapies has its advantages and deficiencies. Retrociliary diathermy acts by altering the circulation of the ciliary body. When properly performed it is harmless and reduces the formation of aqueous to approximately half its initial value. The indications of the procedure have been defined by L. and R. Weekers.[8] Diamox inhibits markedly the formation of aqueous but the required dosage can seldom be tolerated over a long period (Becker,[9] Grant and Trotter,[10] Weekers and Watillon[11]).

We would stress the advantages of *l*-adrenalin in the treatment of open-angle glaucoma. It rarely produces intolerance and can be used for months.[3, 4] Levorotatory adrenalin is definitely contraindicated in narrow-angle glaucoma as the accompanying mydriasis closes the angle, increases re-

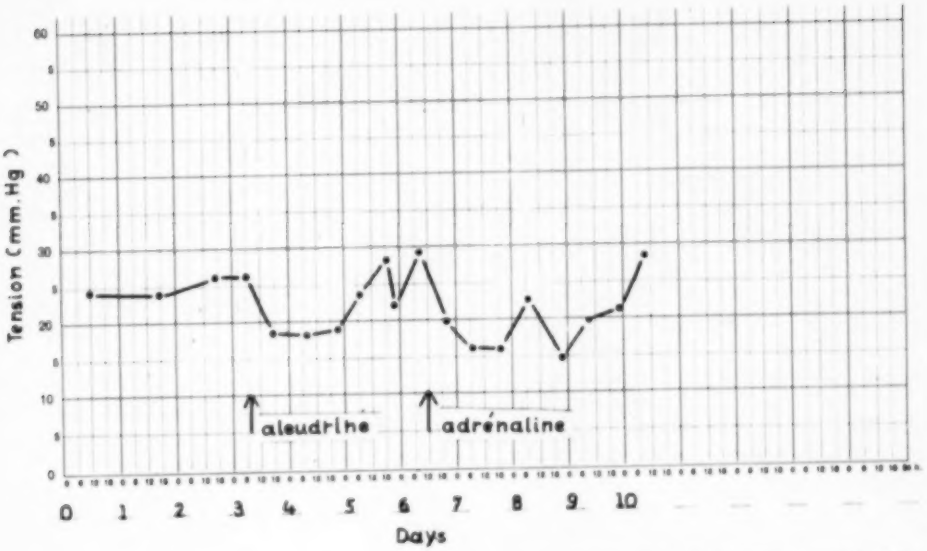


Fig. 1 (Weekers, Delmarcelle, and Gustin). The effect on ocular tension of a single instillation of aleudrine and of a single instillation of *l*-adrenalin in the same patient.

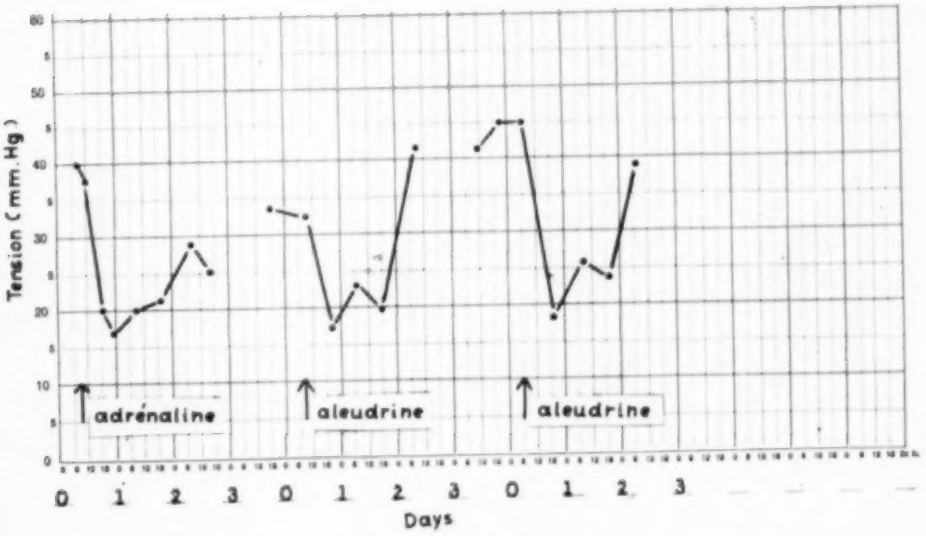


Fig. 2 (Weekers, Delmarcelle, and Gustin). The effect on ocular tension of *l*-adrenalin and aleudrine in the same patient.

sistance to drainage, and raises the ocular tension despite a lessened production of aqueous. This accounts for our special interest in aleudrine, which apparently inhibits the formation of aqueous like *l*-adrenalin but is not a mydriatic. The prolonged use of aleudrine appears contraindicated however because of the tachycardia it provokes.

Summary

1. The reduction of ocular tension effected by *l*-adrenalin in open-angle glaucoma is due to a lessened production of aqueous and not to any increased facility of drainage.

2. The reduction of ocular tension by noradrenalin is less than that achieved by *l*-adrenalin, and the action of *d*-adrenalin and adrenalone is practically nil.

3. Aleudrine, though not a vasoconstrictor, acts like *l*-adrenalin in reducing ocular tension. Since aleudrine also induces no mydriasis it may be eventually of some value in narrow-angle glaucoma, but the drug has the great disadvantage of provoking tachycardia.

4. The advantages accruing from the simultaneous use of remedies facilitating aqueous drainage and reducing aqueous formation are emphasized.

Hôpital de Bavière.

Our thanks are due to Prof. Z. M. Bacq for his most useful suggestions on the selection of sympathomimetic amines and his interest in our work; to Mr. Lejeune, Director of Pharmacy, Hôpital de Bavière, his associate, Mr. Rondia, and Mr. Henrioul, pharmacist, for the preparations of the solutions used in these investigations.

References

1. Hamburger: Experimentelle Glaukomtherapie. Klin. Monatsbl. f. Augenh., **71**:810, 1923.

2. Goldmann, H.: L'origine de l' hypertension oculaire dans le glaucome prémitif. Ann. d' Ocul., **184**: 1086, 1951.

3. Weekers, R., Prijot, E., and Gustin, J.: Recent advances and future prospects in the medical treatment of ocular hypertension. Brit. J. Ophth., **38**:742, 1954.

4. ———: Mesure de la résistance à l'écoulement de l'humeur aqueuse au moyen du tonomètre électronique. 6 me partie: mode d'action de l'adrénaline dans le glaucome chronique. Ophthalmologica, **128**:213, 1954.

5. Langley and MacDonald, R.: Clinical method of observing changes in the rate of flow of aqueous humour in the human eye. Brit. J. Ophth., **36**:432, 1952; **36**:499, 1952.

6. Weekers, R., and Delmarcelle, Y.: Hypotonie oculaire par réduction du débit de l'humeur aqueuse. Ophthalmologica, **125**:425, 1953; **127**:373, 1954.

7. Bacq, Z. M.: Pharmacodynamie biochimique. Sciences et Lettres, Liège, 1954, p. 116.

8. Weekers, L., and Weekers, R.: Les indications de la diathermie rétrociliaire non perforante thermométrique dans le traitement de l' hypertension oculaire. Acta XVI Concilium Ophthalmologicum (Brittania) 1950, p. 950.

9. Becker, B.; Decrease in intraocular pressure in man by a carbonic anhydrase inhibitor: Diamox. Am. J. Ophth., **37**:13, 1954.

10. Grant, W. M., and Trotter, R.: Diamox in treatment of glaucoma. Arch. Ophth., **51**:735, 1954.

11. Weekers, R., and Watillon; M.: Les traitements de l' hypertension oculaire par réduction du débit de l' humeur aqueuse. Bull. Soc. belge ophtal., **108**:507, 1954; and Ann.d' Ocul., in press.

LONG-TERM ADMINISTRATION OF ACETAZOLEAMIDE (DIAMOX) IN THE TREATMENT OF GLAUCOMA*

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A carbonic anhydrase inhibitor, acetazoleamide (2-acetylamino-1, 3, 4, thiadiazole-5-sulfonamide) was developed by Roblin and associates (1950).[1] The proprietary name of the preparation is *Diamox*. Wistrand (1951)[2] showed that the ciliary processes and iris of rabbits contain carbonic anhydrase. Green, Capper, Bocher, and Leopold (1954)[3] reported that Diamox inhibits the carbonic anhydrase activity of the rabbit ciliary body up to a maximum of 93 percent. Kinsey (1953)[4] found an excess of bicarbonate in the aqueous humor as compared to the plasma. Friedenwald (1949)[5] found evidence which suggested that the production of bicarbonate might be involved in the secretion of aqueous. As a result of these and other related experimental observations Diamox was used clinically for the short term treatment of glaucoma[6–11] with the idea that the inhibition of carbonic anhydrase would decrease the secretion of aqueous.

Becker (1954),[6] in a preliminary paper, reported on the initial responses of 21 patients; further observations on 11 of these are included in this present study. These patients are identified in Table 1. Becker[12] showed that the beneficial effects of Diamox in the control of glaucoma are due to an inhibition of the inflow of intraocular fluid without measurable increase in the facility of outflow. He found that the effects of miotics were additive.

The present study was undertaken in order to find out whether Diamox could be administered over a prolonged period for the control of glaucoma. The points specifically investigated were (a) whether a clinically satisfactory reduction of intraocular pressure was maintained during treatment, (b) whether there were any significant changes in aqueous flow and in facility of outflow, (c) whether patients developed a resistance or unresponsiveness to the drug, (d) whether any ocular or systemic complications developed. This study has been under way since October, 1953. Our experience during the first 15 months, ending on January 1, 1955, is here reported.

CASES SELECTED FOR STUDY

The patients reported in this study were almost without exception individuals in whom other forms of treatment, both medical and surgical, had been without effect in controlling the ocular pressure. These 29 patients comprise our total experience to date with long-term Diamox treatment. Twenty of the 29 patients were followed from four to 14 months, an average of 10.5 months. The remaining nine patients included in the series are those who were started on long-term Diamox treatment but in whom treatment could not be continued

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TABLE 1

DATA ON PATIENTS RECEIVING DIAMOX

Patient No.	Age (years) Race & Sex	Diagnosis (Surgery before Diamox treatment)	Months on Diamox	Clinical Control on Diamox		P_{01}	P_{02}
1 WB	43 C M	Primary glaucoma (open angle) OU Diabetes	9	Fair	RE LE	51 43	21 21
2 RW	48 C M	Primary glaucoma (open angle) OU 2 cyclodialysis & cyclodiathermy RE—cyclodialysis LE	8	Good	RE LE	24 30	11 19
3 SH	73 W F	Primary glaucoma (open angle) OU Cyclodiathermy RE, cataract extraction, cyclodialysis with cyclodiathermy, LE	6	Fair	RE LE	27 37	18
4 HW	70 C F	Primary glaucoma (open angle) OU	6	Good	RE LE	53 50	18 23
5 WH*	61 C M	Primary glaucoma (open angle) OU	14	Good	RE LE	37 34	17 17
6 AC*	57 C F	Primary glaucoma (open angle) OU	14	Fair	RE LE	63 52	21 19
7 CH*	46 C F	Primary glaucoma (open angle) OU Diabetes—anterior sclerectomy RE	14	Fair	RE LE	34 25	25 21
8 JV	40 C F	Primary glaucoma (open angle) OU	3	Good	RE LE	46 40	22 18
9 HR	49 C F	Primary glaucoma (open angle) OU Trephine RE, cyclodialysis, LE	9	Good	RE LE	27 40	18 20
10 PB*	62 C F	Primary glaucoma (open angle) OU Trephine LE	14	Good	RE LE	37 15	20 16
11 MW	73 C F	Primary glaucoma (open angle) OU	13	Poor	RE LE	49 53	25 25
12 CM	44 C M	Primary glaucoma (open angle) OU Trephine, cyclodialysis, cyclodiathermy, cataract extraction, LE	4	Good	LE	38	17
13 MB	65 W F	Primary glaucoma (open angle) OU Cyclodiathermy and cataract extraction OU; cyclodialysis, LE	13	Failure	RE LE	20 32	14 17
14 MR	57 C F	Primary glaucoma (open angle) RE cyclodiathermy. Diabetes, and later rubeosis of the iris	2	Failure	RE	45	72
15 GB	52 C F	Primary glaucoma (open angle) OU cyclodiathermy RE; cyclodialysis and cyclodiathermy LE	3	Failure	RE	53	33–52
16 MK	56 W F	Primary glaucoma (narrow-angle) RE absolute glaucoma, LE; cataract extraction, 2 cyclodialysis RE	8	Good Fair	RE LE	46 38	19 23
17 MD*	81 C F	Secondary glaucoma following cataract extraction RE; normal LE	13	Good	RE LE	51 17	19 11
18 RJ	49 C F	Secondary glaucoma following uveitis, OU	9	Fair	RE LE	46 48	20 17

* Indicates patients included in Dr. Becker's preliminary report.

TABLE 1—(*Continued*)

Patient No.	Age (years) Race & Sex	Diagnosis (Surgery before Diamox treatment)	Months on Diamox	Clinical Control on Diamox		P_{si}	P_{sr}
19 RG*	58 C M	Secondary glaucoma following uveitis, OU; cyc odiathermy, LE	9	Good	RE LE	42 48	18 19
20 CW*	25 C F	Secondary glaucoma following congenital lues with interstitial keratitis, OU; basal iridectomy cyclodiathermy, OU	13	Fair	RE LE	43 43	22 22
21 MH*	41 C F	Secondary glaucoma following uveitis; iridectomy, cyclodialysis trephine and cycloelectrolysis, RE	14	Good	RE	38	22
22 TM*	33 C M	Secondary glaucoma (+TPI and chorioretinal lesions); iridencleisis OU, cyclodialysis, cyclodiathermy, LE	14	Good	RE LE	34 20	12 8
23 BB	52 C F	Secondary glaucoma (uveitis) sclerectomy, OU	6	Failure	RE LE	63 61	43 28
24 GC	46 C F	Secondary glaucoma (congenital cataract) discission, cyclodialysis, RE; discission, cyclodialysis trephine, LE	6	Poor	RE LE	46 25	27 22
25 CRH*	45 W M	Secondary glaucoma (uveitis) cyclodialysis, iridencleisis, RE	2	Failure	RE	38	24
26 FK	40 W M	Secondary glaucoma (uveitis) RE iridectomy, RE		Failure	RE	34	24
27 EM	83 W M	Secondary glaucoma (uveitis) OU. Trephine, OU	$\frac{1}{2}$	Failure	RE LE	49 18	22 12
28 EU	47 W F	Secondary glaucoma (congenital lues) cyclodialysis, sclerectomy RE	1	Failure	RE LE	53 32	41 21
29 MG*	66 C F	Secondary glaucoma (cataract extraction) OU; diabetes; sclerectomy cyclodialysis, RE; cyclodiathermy, LE	1	Failure	RE LE	76 74	3–15 25–54

to the end of the study (January 1, 1955). The reasons why Diamox treatment was discontinued in these patients are presented later.

The 29 patients involved 56 eyes. Of these, 18 had clear lenses, 27 had lens opacities, and 11 were aphakic. Two eyes were in absolute glaucoma and two eyes were entirely normal, with no change in vision, fields, or facility of outflow. The race, sex, type of glaucoma, and previous surgery are detailed in Table 1.

Program of Treatment

The majority of the patients were started on one 250-mg. Diamox tablet every six hours, night and day. Two patients (Cases 7 and 11) were given smaller doses more frequently. No patient was given a maintenance dose of higher than one gm. in 24 hours. No systematic attempt was made to explore the possibilities of lower dosage.

Some months after the beginning of this study, an enteric-coated, 250-mg. Diamox capsule became available. Eighteen patients were placed on the routine of one 250-mg. tablet and one enteric-coated, 250-mg. capsule simultaneously every 12 hours for a major portion of their treatment.

All patients were given miotics during their treatment with Diamox, usually pilocarpine (two percent) or eserine (0.25 percent).

Program of study

All the patients in this series were outpatients. In order to determine the initial effect of Diamox and whether this effect was maintained, as a trial procedure the tension was checked hourly from the third to the ninth hour after administration of the Diamox tablet. Similar observations were repeated on each patient several times during the course of the study. Occasionally, there was an opportunity to examine these patients in the evening or night. Diurnal variation appeared to play much less role in the level of the intraocular pressure than did the time elapsed since the last dose of Diamox. After it had been demonstrated that Diamox had produced a satisfactory reduction of the tension, the intraocular pressure was checked every two to four weeks. Complete eye examinations were made in all patients every four to six weeks. Whenever possible, tonography was performed before the administration of Diamox and was repeated at intervals throughout the treatment. Systemic side effects were searched for and recorded at each visit. Blood and urine were examined monthly.

Results

A. Control of ocular tension

1. Control of daily pressure variations

The first Diamox effect was noted 20 minutes after the administration of a 250-mg. tablet and the reduction of tension was maintained for about six hours. The enteric-coated, 250-mg. capsules became effective six hours after ingestion and the reduction of tension was then maintained another six hours. Combined treatment with one regular tablet and one enteric capsule every 12 hours gave an effect equal to that obtained by one regular tablet every six hours. With these dosage schedules there were no high peaks in the intraocular pressure during the course of the day.

2. Evaluation of clinical control

Clinical control was evaluated on the basis of preservation of vision, visual fields, and the maintenance of ocular tension within normal limits. All intraocular pressures recorded in this study were based on the new calibration tables of the Committee on Standardization of Tonometers (1954).[13] These estimates for pressure are generally 3.0 to 6.0 mm. Hg lower than those made with the previous tables.

Twenty of the 29 patients were continued on Diamox to the close of the study, January 1, 1955. In this group the results are as follows (table 2):

The two patients with poor response were considered inoperable. They were therefore continued on long-term Diamox therapy. In one of these cases, this therapy was accompanied by a satisfactory reduction in the ocular tension but vision continued to fail and the visual fields became further constricted. In the other, Diamox did not fully control the tension. Of these 20 patients, eight initially had fields of less than 15 degrees in each eye. Five of these patients with constricted fields showed good response to long-term Diamox therapy, two showed a fair response, and one a poor response.

There were nine patients in whom the long-term therapy was abandoned. These are classified in Table 1 as failures. Five

TABLE 2

Results in 20 patients continued on Diamox to close of study

No. of Cases	Results	Criteria for Results
12	Good	Intraocular pressure below 24 mm. Hg in both eyes with preservation of vision and field in both eyes.
6	Fair	Borderline intraocular pressure (24–30 mm. Hg) the same or lower pressure in the other eye, vision, and field essentially unchanged in both eyes.
2	Poor	Intraocular pressure above 30 mm. Hg in one eye or significant loss of vision or field in one eye.

of these patients were never satisfactorily controlled on Diamox and miotics, and glaucoma surgery was performed within three months of the beginning of their Diamox treatment. Nevertheless, four of these five had significantly lower pressures on Diamox therapy than they did before treatment. The fifth patient (Case 14) was a Negro diabetic with open-angle glaucoma and some rubeosis of the iris.

B. Changes in facility of outflow

The coefficient of facility of outflow and the rate of aqueous flow were determined prior to treatment and during the course of treatment whenever possible. Initially these determinations were made approximately every two weeks and later every six weeks. The results of these studies are detailed in Table 3.

TABLE 3

Results of study on facility of outflow

Case No.		P_{01}	C_1	F_1	P_{02}	C_2	F_2	$-\%\Delta F$	C_{last}	C_{last}/C_1
1 WB	RE	51	0.07	2.80	21	0.09	0.90	68	0.10	1.43
	LE	43	0.10	3.20	21	0.09	0.90	72	0.15	1.50
2 RW	RE	24	0.10	1.30	11	0.11	—	—	0.10	1.00
	LE	30	0.11	1.98	19	0.09	0.72	64	0.08	0.73
3 SH	RE	27	0.19	3.04	18	0.15	1.05	66	0.15	0.79
	LE	37	0.11	2.86	27	0.10	1.60	44	0.10	0.91
4 HW	RE	53	0.05	2.10	18	0.03	0.21	90	0.03	0.60
	LE	50	0.08	3.12	23	0.04	0.48	85	0.04	0.50
5 WH	RE	37	0.05	1.30	17	0.08	0.48	63	0.08	1.60
	LE	34	0.14	3.22	17	0.10	0.60	81	0.07	0.50
6 AC	RE	63	0.07	3.64	21	0.06	0.60	84	0.06	0.86
7 CH	RE	34	0.06	1.38	25	0.08	1.12	19	0.07	1.17
	LE	25	0.10	1.40	21	0.11	1.10	21	0.10	1.00
8 JV	RE	46	0.04	1.40	22	0.08	0.88	37	0.09	2.25
	LE	40	0.04	1.16	18	0.10	0.70	40	0.12	3.00
10 PB	RE	37	0.13	3.38	20	0.09	0.81	76	0.09	0.69
	LE	15	0.15	0.60	16	0.09	0.45	25	0.09	0.60
17 MD	RE	51	0.06	2.40	19	0.10	0.80	67	0.06	1.00
	LE	14	0.22	0.66	11	0.19	—	—	0.15	0.68
18 RJ	RE	46	0.07	2.44	20	0.10	0.90	64	0.10	1.43
	LE	48	0.07	2.60	17	0.11	0.66	75	0.11	1.57
22 TM	RE	34	0.10	2.30	12	0.10	—	—	0.09	0.90
	LE	20	0.11	0.99	8	0.10	—	—	0.10	0.91
Mean		37.3	0.10	2.14	18.3	0.10	0.79	60	0.09	1.11
Standard deviation		12.8	0.05	0.93	4.6	0.03	0.31	22	0.03	0.59
Standard error of mean		2.7	0.01	0.20	0.9	0.01	0.07	5	0.01	0.12

Correlation coefficient for F_1 and $F_2 = 0.113$ (19 pairs of values)
Correlation coefficient for $-\%\Delta F$ and $F_1 = 0.757$ ($P = 0.01$)

Explanation for Table 3

P_0 = intraocular pressure in mm. Hg
C = facility of outflow in mm.³/min./mm. Hg
F = aqueous flow in mm.³/min.

$$\%\Delta F = 100\,\frac{F_2 - F_1}{F_1}$$

Subscript $_1$ = value before Diamox
Subscript $_2$ = average value during Diamox
Subscript $_{last}$ = last value obtained during Diamox.

C was measured by Grant's technique (1950).[34] $F = C(P_0 - P_v)$ where P_v is episcleral venous pressure and was taken as 11 mm. Hg. Linnér (1955).[38] No calculations were made for flow when P_0 was less than 13 mm. Hg.

There was no statistically significant difference between the facility of outflow prior to treatment and that shown throughout the course of treatment. Diamox depressed the rate of aqueous flow from an average pretreatment level of 2.14 ± 0.20 mm.^{3}/min. to an average of 0.79 ± 0.07 mm.^{3}/min. Previous studies have shown that the rate of aqueous flow is usually not depressed still further by increases in the dosage of Diamox. Thus there exists a residual flow insensitive to Diamox, and this suggests that some patients with very little aqueous flow might be relatively resistant to Diamox, as found by Becker.[7] No such resistant cases were included in the present series, because only those patients with a satisfactory initial response to Diamox were selected for long term therapy. In the individual patient, the level of aqueous flow during treatment was always lower than the pretreatment level, but otherwise was entirely independent of the pretreatment aqueous flow. This is illustrated in Figure 1. Thus it is not surprising that a low initial flow was associated with a low percent inhibition of flow.*

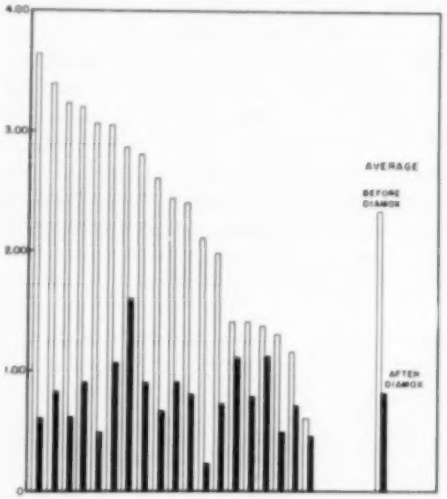

Fig. 1 (Kupfer, Lawrence, and Linnér). Rate of flow of intraocular fluid in cubic millimeters per minute estimated in 19 eyes before (open rectangles) and after onset of Diamox therapy (solid rectangles).

C. Resistance to Diamox

Two patients (Cases 10 and 11) developed a slow rise in tension (March, 1955) after 16 and 15 months of Diamox therapy. When their Diamox was discontinued, their tension did not rise further. At this time, their facility of outflow and rate of aqueous flow (both with and without Diamox) were much lower than pretreatment levels. Their diminished facility of outflow probably was a genuine progression of their glaucomatous process. No conclusion is made as to whether this progression was facilitated by the therapy or occurred entirely independently. When these patients became resistant to Diamox, their aqueous flow (both with and without Diamox) was comparable to their flow earlier in their treatment when their pressure was under good control. This suggests that their rate of aqueous flow had diminished to the level at which the physiologic systems inhibited by Diamox are no longer bottlenecks in the secretory process. Thus the resistance of these patients may not represent a true tolerance to Diamox. In all other cases, once a therapeutic effect on the tension had been observed, this reduction in tension was maintained during the entire period of treatment, and there was no evidence of any developing resistance to the drug.

D. Complications

Two patients developed central scotomas while under treatment and the Diamox was discontinued. One (Case 25) was that of a 45-year-old white man with uveitis of unknown etiology and secondary glaucoma. This patient developed loss of vision, a central scotoma, and some visible macular changes in his only eye after two months of Diamox. During the six months after discontinuing the Diamox, his vision slowly cleared, his central field became normal, and

* See explanation for Table 3.

the macular changes disappeared. The other patient (Case 13) was a 60-year-old white woman who developed a central scotoma without visible macular change after 10 months of Diamox. During the succeeding six months without Diamox there was some diminution in the size of the scotoma and her central vision improved from 20/200 to 20/80. No change was noted in the appearance of her fundi.

One patient (Case 22) developed a peripheral occlusion of a lower temporal retinal vein after four months of treatment. Diamox was withheld for 10 days, and was then administered uneventfully for eight months more. The patient did not lose vision or field, and the ocular pressure, which rose on withdrawal of the drug, remained well-controlled after it was readministered.

Two patients discontinued Diamox because of systemic side effects. One case (26) was that of a 40-year-old fireman who found himself weakened and short of breath on high ladders. The other (Case 27) was an enfeebled 84-year-old man who had been able to get out of bed for a short time each day before starting Diamox and who felt too weak to leave his bed during the Diamox treatment.

The majority of the patients noticed some mild general symptoms. These were usually insufficient to provoke a spontaneous complaint, and the slight side effects were revealed only by careful questioning. The symptoms most frequently complained of were numbness and tingling of hands and feet, slight loss of appetite, and minimal weakness or shortness of breath on exertion. These symptoms did not tend to increase during the study. In some patients, these symptoms subjectively decreased as the treatment was continued. No skin rashes or changes in blood or urine were discerned.

Discussion

A great number of the patients in this series were Negroes, the majority of whom had undergone previous glaucoma surgery without benefit; Diamox and miotics were their last recourse. It is, therefore, not surprising that this group of patients did not complain. Less stoical patients in less desperate conditions may be expected to be less tolerant of side effects.

Carbonic anhydrase has been shown to be present in mammalian lens, ciliary body, and retina.[16, 17] Therefore, the patients in this series were carefully examined for possible complications in the lens and the retina occurring in the course of therapy. There was no evidence that any of the patients developed lens opacities under therapy. It is difficult to evaluate the importance of the central scotomas in two patients and the branch vein occlusion. These are reported as observed complications without any conclusion as to whether they represent effects of the therapy. A group of patients with such advanced glaucoma followed for over 10 months can be expected to develop some complications under any form of therapy.

The absence of demonstrable ocular or systemic toxicity in this long-term Diamox administration is, of course, no guarantee that complications will not occur if more patients are followed for longer periods. However, in this series most patients tolerated continued Diamox administration without ocular or systemic complications. The addition of Diamox to the therapeutic armamentarium resulted in good control of the intraocular pressure for a protracted period in some patients whose visual prognosis would have been extremely poor on other forms of therapy.

Goldmann[18] reported several patients with filtering wounds after cataract extractions and cyclodialyses who later developed intractable glaucoma when the cicatrices became closed. He hypothesized that this might be a result of disuse atrophy of the natural outflow channels. It seemed possible that a similar process might occur in the abnormal outflow channels of this group of patients when the aqueous flow was reduced by Diamox treatment. However, the average

facility of outflow was not reduced in these patients during the study. As previously noted, two patients developed marked reduction in facility of outflow in March, 1955.

Summary

A group of 29 patients with advanced glaucoma of different types were given long-term treatment with Diamox and miotics. Twenty of these were treated an average of 10 and a half months with Diamox. Of these, 12 were classed as being under good control, six as under fair control, and two as under poor control. Of the remaining nine, five patients required surgery before the close of the study, two patients developed central scotomas (one with visible macular change) while under Diamox therapy, and two patients discontinued the drug because of shortness of breath and weakness. Two patients developed a late resistance to Diamox treatment.

It is felt that the long-term use of Diamox can be a useful adjunct in the treatment of advanced glaucoma. There remains the possibility that significant complications will be revealed by a larger series of patients and by a longer period of treatment.

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References

1. Miller, W. H., Desser, A. N., and Roblin, R. O., Jr.: Heterocyclic sulfonamide as carbonic anhydrase inhibitors. J. Am. Chem. Soc., **72**:4893, 1950.

2. Wistrand, P. J.: Carbonic anhydrase in the anterior uvea of the rabbit. Acta Physiol. Scandinav., **24**:144, 1951.

3. Green, H., Capper, S. A., Bocher, S. A., and Leopold, I. H.: Effect of acetazoleamide (Diamox) on the carbonic anhydrase activity of the anterior uvea of the rabbit eye. Arch. Ophth., **52**:758-762 (Nov.) 1954.

4. Kinsey, V. E.: Comparative chemistry of aqueous humor in posterior and anterior chambers of rabbit eyes. Arch. Ophth., **50**:401, 1953.

5. Friedenwald, J. S.: Formation of intraocular fluid. Am. J. Ophth., **32**:9 (June) 1949.

6. Becker, B.: Decrease in intraocular pressure in man by a carbonic anhydrase inhibitor, Diamox. Am. J. Ophth., **37**:13-15, 1954.

7. ———: The short-term administration of Diamox in the therapy of the glaucomas. To be published in 1955.

8. Breinin, G. M., and Gortz, H.: Carbonic anhydrase inhibitor acetazoleamide (Diamox). Arch. Ophth., **52**:333 (Sept.) 1954.

9. Grant, W. M., and Trotter, R. R.: Diamox (acetazoleamide) in the treatment of glaucoma. Arch. Ophth., **51**:735-739 (June) 1954.

10. Kleinert, H.: Die Beeinflussung pathologischer Augendrucksteigerungen mit Diamox, einem neuartigen Diuretikum. Klin. Monatsbl. f. Augenh., **125**:271-279, 1954.

11. Posner, A.: The action of Diamox in narrow-angle glaucoma and related conditions. EENT Monthly, **33**:366, 1954.

12. Becker, B.: The evaluation of glaucoma therapy by tonography. To be published.

13. Friedenwald, J. S.: Decennial report by the Committee on Standardization of Tonometers. Supplement of the Am. Acad. Ophth., Chap. 7, p. 94, 1954.

14. Grant, W. M.: Tonographic method for measuring facility and rate of aqueous flow in human eyes. Arch. Ophth., **44**:204, 1950.

15. Linnér, E.: The outflow pressure in normal and glaucomatous eyes. Acta Ophth., **33**:101, 1955.

16. Bakker, A.: Der Kohlensaureanhydrasegehalt verschiedener Augengewebe einiger Saugetiere. Ophthalmologica, **102**:351-360, 1941.

17. ———: Carbonic anhydrase and cataracta lentis. Brit. J. Ophth., **32**:910-912, 1948.

18. Goldmann, H.: Klinische Studien zum Glaucomproblem: I. Schicksal des Schlemmschen. Abfluss-Systems nach Schaffung neuer Abflusswege. Ophthalmologica, **125**:16-21, 1953.

THE VALUE OF HEREDITY IN THE DETECTION AND STUDY OF GLAUCOMA*

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Great strides have been made in recent years in the methods of early diagnosis and treatment of glaucoma. For the prevention of blindness from glaucoma, these methods should be applied in the earliest possible stage of the disease. Unfortunately, in this stage symptoms are often lacking in chronic simple glaucoma and may be so atypical in narrow-angle glaucoma as to be disregarded by the patient and misinterpreted by the physician.

One approach to the problem of detecting cases of glaucoma in the early stages is the use of appropriate screening methods applied to various population groups. A survey by Brav and Kirber[1] of 10,000 adults in the general population over 40 years of age yielded an incidence of glaucoma of 1.53 percent, which included borderline cases. It occurred to us that similar screening methods could be applied more advantageously to selected groups in which a higher incidence of glaucoma can be anticipated.

Investigations in the heredity of glaucoma have shown strong familial tendencies in this disease. Biro[2] found a positive family history in 5.6 percent of 761 cases; Posner and Schlossman[3] reported familial tendencies in 13.7 percent of 373 patients; and in Probert's[4] series of 571 patients blind from primary glaucoma, the incidence of familial glaucoma was 17.8 percent.

These figures refer to the percentage of families in which glaucoma occurs in more than one member. Clinically, these familial cases have no distinctive characteristics when compared with glaucoma cases in general. The high familial incidence of glaucoma suggested that the relatives of glaucoma patients constitute a group in whom a high incidence of undiagnosed glaucoma is to be expected.

This study was undertaken to determine how many unsuspected glaucoma cases could be found on screening a group of such relatives. In addition, our results indicated the value of applying genetics in a study of certain phases of glaucoma, especially the role of the narrow angle.

METHODS

The present survey is based on the findings in 199 patients with primary glaucoma and 192 of their relatives. Patients with known primary glaucoma who were attending the Glaucoma Clinic of the Manhattan Eye, Ear, and Throat Hospital were interviewed and a careful family history was obtained with special reference to glaucoma and other eye diseases. A diagram of the family pedigree was prepared. On this were noted the ages of all living members, the ages attained by those deceased, diagnoses of eye diseases when known, and the ages of onset of the diseases and of blindness (fig. 1).

The patient's records were reviewed and were supplemented by further examinations whenever necessary. All the living relatives were contacted either through the patient or directly by a medical social worker and were asked to come to the clinic for a single screening examination without fee. In addition, several persons who knew of glaucoma in their families were referred to us directly.

In the examination of the relatives, any history of eye complaints was noted, further

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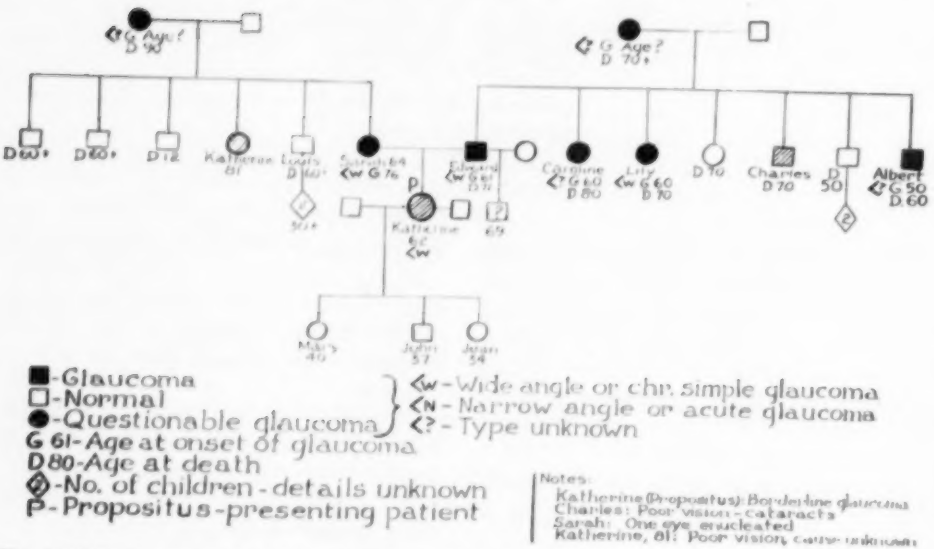

Fig. 1 (Kellerman and Posner). Sample pedigree of a glaucoma family, showing dominant inheritance.

information concerning the family pedigree was elicited, and the salient characteristics of the eyes in reference to glaucoma were recorded. The following points were noted: the presence and type of ametropia as judged by the glasses worn, the depth of the anterior chamber and the width of the chamber angle as estimated with the slitlamp, the type of the physiologic cupping of the disc, the presence of pathologic cupping and pallor, and the ocular tension as measured with a standard Schiøtz tonometer (7.5-gm. weight). All tension measurements were made with the same recently calibrated tonometer. When any suspicion of glaucoma arose, the relative was asked to return for further tests which included visual fields, tonography, repeated tonometry, rigidity estimation, and the indicated provocative tests.

The following findings were considered suspicious: tension over 28 mm. Hg,* a difference of 5.0 mm. Hg or more between the tensions of the two eyes, narrow chamber angles, pathologic or possibly pathologic cupping, pallor of the optic nerveheads, and a strongly dominant glaucoma strain in the family. A dark-room provocative test was performed on every individual with narrow angles, even if there were no other signs of glaucoma.

In general, those whose tensions repeatedly measured between 28 and 32 mm. Hg and who had no other positve findings were considered as borderline cases. A positive diagnosis of glaucoma was made only if there were two or more distinctly abnormal findings. In cases in which a definite diagnosis of glaucoma was made and which were followed for one year or more, the subsequent clinical course corroborated our diagnosis. The patients who required observation or treatment were referred to their own ophthalmologists or clinics.

Observations

We examined 192 relatives of patients with primary glaucoma. The age range of these relatives was from one to 75 years and the majority were persons whose one or both parents had glaucoma. The others were siblings, nieces and nephews, and grandchildren. Of the 192 relatives, eight (or four percent)

* Schiøtz-Friedenwald conversion table of 1948.

were found to have definite primary glaucoma, all of the chronic simple type. There were four men and four women in this group. One man had glaucoma in an advanced stage with optic atrophy; the other seven were in very early stages of the disease, with minimal or no visual field changes. None of these seven had any previous inkling of disease in their eyes. Six of the eight patients with discovered glaucoma had the disease in both eyes.

Eleven relatives showed findings that aroused a strong suspicion of the presence of glaucoma, but no definite proof of the disease could be obtained. For the most part, these were people whose ocular tensions ranged from 28 to 32 mm. Hg and in whom the results of provocative tests were equivocal or whose coefficients of outflow were low. This borderline group included two persons in whom a narrow-angle type of glaucoma was suspected. Of those relatives who were not included in either the glaucomatous or borderline groups, three showed a tension difference of five mm. Hg or more between the two eyes, and one relative had episodes that were considered to be glaucomatocyclitic crises.

While only 22 of the 192 relatives examined were past the age of 60 years, four of the eight definite glaucomas discovered belonged to this older age group. The ages of the remaining four ranged from 50 to 33 years. Of the eight, six had one glaucomatous parent and the other two had siblings with glaucoma. In five of the six with glaucomatous parents, the condition was diagnosed at an earlier age than in the parents. The most extreme example of this "anticipation" phenomenon was the discovery of glaucoma in a 33-year-old man whose father's glaucoma had been diagnosed at the age of 65 years. Analysis of the pedigrees of the eight newly discovered cases showed that in seven families only one relative was known to be affected. Of the 11 borderline cases, five were offspring of glaucomatous parents, and were considerably younger than their parents had been at the time when the diagnosis of glaucoma was made. Two of this group of 11 had pedigrees that indicated a dominant mode of transmission and each of two other families had two affected relatives.

Altogether, 248 pedigrees were collected, among which 34 persons seemed to show a dominant glaucomatous trait. Our figures as to the incidence of familial glaucoma based on the family history tended to confirm those of Posner and Schlossman, and Probert. Twenty-seven, or 13.5 percent of 199 glaucoma patients interviewed in this study gave a positive family history of glaucoma and 11 patients (5.5 percent) gave questionably positive histories.

One of the aspects of glaucoma brought into focus by this study was the pattern of ocular tensions within those families in which glaucoma was present. In the great majority of the relatives the tensions measured between 20 and 24 mm. Hg. This is similar to the average tensions found in the general population. The tensions within each family varied considerably, the standard deviation from the mean tension being 2.05 mm. Hg. Of 359 eyes, 61 had tensions of 25 mm. Hg or over. Of these, 32 were in the discovered and borderline groups, leaving 327 eyes that were considered as nonglaucomatous. Among these 327 eyes were 29 eyes (8.9 percent) with tensions of 25 mm. Hg and over. The 45 normal members of the families with discovered and borderline cases of glaucoma account for 11 of these high normal tensions. Thus the incidence of high normal tensions in these families is 24.4 percent as compared with an incidence of 6.4 percent in families where no glaucoma was discovered. This difference is statistically significant and suggests the presence of potentially glaucomatous cases in those families where glaucoma has already been discovered. This statistical concept is the closest approximation to a recognition of a truly preclinical stage of glaucoma. It lends special significance to those individuals with a high

normal tension who belong to families in which glaucoma is genetically dominant.

Starting with the assumption, well founded on clinical experience,[5, 6] that acute narrow-angle glaucoma shows familial tendencies, we attempted to find out whether the narrow angle is likely to be the inherited characteristic responsible for the transmission of the disease.

The incidence of narrow angles in the relatives of patients with chronic simple glaucoma was compared to the incidence of narrow angles in the relatives of patients with acute congestive glaucoma. Of 181 eyes of relatives of chronic simple glaucoma patients, 12, or seven percent, had narrow angles; whereas, among 48 eyes of relatives of acute congestive glaucoma patients, 12, or 25 percent, showed narrow angles. This is in essential agreement with the findings recently reported by Törnquist,[6] who presented evidence that the depth of the anterior chamber is genetically determined and that a shallow anterior chamber is more frequently found among relatives of patients with acute glaucoma than in the population at large.

The ocular tensions in the eyes of acute glaucoma relatives tended to be in the low normal range, none being over 23 mm. Hg. This group contrasts sharply with the group of the relatives of chronic simple glaucoma patients, where the angles were wide and tensions frequently tended to be elevated.

The high incidence of narrow angles in the relatives of narrow-angle glaucoma patients points to the hereditary nature of this characteristic. These observations offer support for the concept that chronic simple glaucoma and narrow-angle glaucoma are separate diseases.

The findings discussed in the preceding sections are summarized in Tables 1 and 2.

TABLE 1

FINDINGS IN RELATIVES OF GLAUCOMA PATIENTS

	Number	Percent
Relatives of glaucoma patients examined	192	100
Discovered cases of glaucoma in the relatives	8	4
Discovered cases of borderline glaucoma	11	5.7
Total eyes examined	359	
Nonglaucomatous eyes	327	
Nonglaucomatous eyes in families of discovered glaucoma cases (all chronic simple type)	45	
Eyes with high normal tensions (between 25 and 30 mm. Hg) in these families	11	24.4
Nonglaucomatous eyes in families without discovered glaucoma	282	
Eyes with high normal tensions in these families	18	6.4

SUMMARY

In this study, a positive family history of glaucoma was obtained in 13.5 percent of 199 patients with primary glaucoma. Of the 192 of their relatives who were examined, eight (or four percent) were found to have definite primary glaucoma. All cases were of the chronic simple type. Eleven (or 5.5 percent) were considered borderline cases. None of the patients whose glaucoma was discovered had any awareness of disease in their eyes and all but one were in a very early stage of glaucoma. The incidence of glaucoma in unselected samples of the general adult population has been variously estimated to be from 0.5 to two percent.

TABLE 2

RESULTS OF STUDY OF CHAMBER ANGLES

	Number	Percent
Eyes examined of relatives of chronic simple glaucoma patients	181	
Eyes with narrow angles in these relatives	12	7.0
Eyes examined of relatives of patients with acute congestive glaucoma	48	
Eyes with narrow angles in these relatives	12	25
Pedigrees derived from glaucoma patients	199	
Positive family history in these pedigrees	27	13.5

Our results show that, for purposes of glaucoma case finding, the relatives of glaucoma patients constitute a group with a high incidence of unsuspected glaucoma. Of a total of 257 pedigrees obtained, 34 indicated the dominant mode of transmission.

Among members of families in which acute glaucoma had occurred we found a much higher incidence of narrow chamber angles than in the over-all group. This suggests that a narrow chamber angle may be an inherited anatomic characteristic, predisposing the eye to narrow-angle glaucoma.

Among the normal members of families in which new cases of chronic simple glaucoma were discovered, the incidence of tensions of 25 mm. Hg and over was significantly higher than in the families with only one affected member. High normal tension may thus be suggestive of a preclinical phase of chronic simple glaucoma, especially where familial tendencies are present.

If borne out by studies on larger samples, these observations should strengthen the concept that chronic simple glaucoma and narrow-angle glaucoma are separate diseases, both clinically and genetically.

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References

1. Bray, S. S., and Kirber, H. P.: Mass screening for glaucoma. J.A.M.A., **147**:1127 (Nov.) 1951.
2. Biro, I.: Notes on heredity of glaucoma. Ophthalmologica, **98**:43, 1939.
3. Posner, A., and Schlossman, A.: Role of inheritance of glaucoma. Arch. Ophth., **41**:125 (Feb.) 1949.
4. Probert, L. A.: A survey of hereditary glaucoma. Canad. M.A.J., **66**:563 (June) 1952.
5. Barkan, O.: Choice of operation in glacouma. Am. J. Ophth., **24**:768, 1941.
6. Törnquist, R.: Shallow anterior chamber in acute glaucoma. Acta Ophth., 1953, Supp. 39.

MONOCULAR NYSTAGMUS*

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In the normal person all eye movements, including those of induced nystagmus, are binocular. The oscillation of the eyes in nystagmus is always conjugate; that is, both globes move simultaneously in the same direction and to the same extent. Dissociation of movements therefore implies some sort of an abnormality. Thus, the movements of the two eyes may differ in amplitude, rate, and direction. For example, in congenital forms, in those resulting from eye disease, and in some acquired lesions of the brainstem, the characteristics of the nystagmus may be different in the two eyes.[1]

A rare form of dissociation is monocular nystagmus on direct forward gaze, in which there is nystagmus in only one eye when the patient looks straight ahead. Excluding total external ophthalmoplegia, we have encountered acquired monocular nystagmus three times in the past three years. It is these cases which form the basis of this report.

Materials and Methods

Of the three patients with monocular nystagmus, two had multiple sclerosis and one had a brainstem disorder of unknown etiology. The ocular movements were investigated by means of electrical recording, employing the method previously described by us.[2]

* From the Department of Neurology, New York University-Bellevue Medical Center, and the Department of Neurology of The Mount Sinai Hospital. This work was aided in part by the Neurologic Research Fund of The Mount Sinai Hospital and in part by a grant-in-aid from the National Multiple Sclerosis Society.

Visual acuity was tested in the first case (B. E.) by Snellen chart and newspaper reading at 15 inches, starting with large headlines, then subheads, and finally standard body type. In Cases 2 and 3, instead of the Snellen chart, a special test was improvised so that it could be employed easily during the administration of a drug (amobarbital sodium) and the simultaneous recording of the ocular movements.

A milk-glass screen, 18 by 18 inches (45 by 45 cm.) was placed four feet (120 cm.) away from the patient at eye level. On it was drawn a red circle around four large and small digits (fig. 1). With the uninvolved eye covered the patient was asked to look straight ahead and report what he saw.

In addition to the usual examination of visual acuity, funduscopy, and direct observations of the extraocular movements, each patient was studied under the following conditions with simultaneous electrical recording of eye movements: (1) Opticomotor stimulation; (2) cold caloric stimulation of the ears; (3) eye closing—unilateral and bilateral; (4) absolute darkness with eyes open; and (5) intravenous barbiturates.

Case reports and results

Case 1

This patient (B. E.), aged 30 years, who presented all the clinical criteria for the diagnosis of multiple sclerosis, complained of "nearsightedness" in the right eye of three years' duration.

Examination revealed pallor of the right optic disc. The left optic disc appeared normal. When the left eye was covered, she described objects as "bobbing up and down" (oscillopsia) and could make out only large objects and headline-sized type. In the right eye the acuity was 20/200 and there was no central scotoma. The vision in the left eye was 20/20.

Fig. 1 (Nathanson, Bergman, and Bender). Special test figure on milk-glass screen used for testing visual acuity.

Monocular nystagmus. A vertical pendular nystagmus, present in all directions of gaze, was noted in the right eye only. There was no nystagmus in the left eye in any position. The electrical record of the nystagmus on direct forward gaze showed regular sinusoidal waves at four cycles per second in the vertical plane of the right eye only (fig. 2). On right lateral and downward gazes, there was no change in rate and character of the nystagmus in the right eye. On upward and left gazes the nystagmus disappeared for short periods and returned in bursts at approximately the same rate, but with some decomposition of the sinusoidal character. The left eye showed no nystagmus. Convergence failed to alter the rate of the nystagmus but increased the amplitude.

Optokinetic nystagmus. Opticomotor stimulation, using a revolving striped drum, produced the expected nystagmus in the horizontal planes, while the monocular vertical nystagmus of the right eye was no longer apparent. When the stripes were traveling upward, the expected opticomotor binocular nystagmus was not elicited. There was only the spontaneous vertical nystagmus of the right eye and this showed a decrease in amplitude. When the stripes traveled downward, typical binocular nystagmus was produced and the monocular vertical nystagmus in the right eye no longer could be detected. In summary, the monocular nystagmus was obliterated in the planes (horizontal and downward) where opticomotor nystagmus was elicited, and persisted where the patient was unable to follow the stripes (upward).

Caloric stimulation (cold water) produced normal coarse, horizontal nystagmus with quick and slow phases on stimulation of either ear. However, when the left ear was stimulated the record showed a persistence of the vertical nystagmus during the height of the caloric response, as illustrated in Figure 3.

Effect of barbiturates. After receiving 150 mg. of amobarbital sodium intravenously, the patient stated that everything was "still" and "clear." Forty seconds later, no trace of nystagmus could be seen on the record. The visual acuity which was 20/200 became 20/50 in the right eye, and she was able to read newspaper body type with few errors. There was no scotoma despite the visual acuity being 20/50. According to the patient's report, her visual disturbance did not return to its previous state until 24 hours later, although a slight vertical nystagmus could be seen reappearing in the right eye 30 minutes after the completion of the injection. On lateral and vertical gazes the typical barbiturate nystagmus was produced in both eyes.

Case 2

The patient (F. G.), aged 31 years, gave a one-year history of decreasing auditory acuity on the right. Four months later there was a sudden onset of "jumping" vision. She stated that this was present when both eyes were open. However, if the left eye was covered, objects upon which she was fixing did not appear to jump. When the right eye

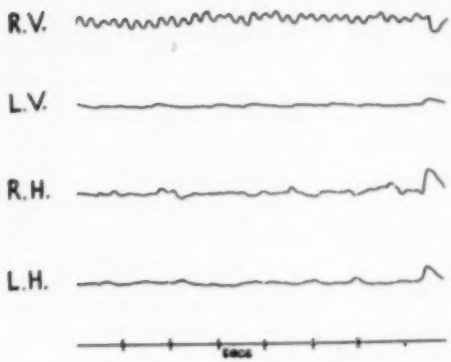

Fig. 2 (Nathanson, Bergman, and Bender). *Case 1 (B. E.).* Electrical recording of the eyes on direct forward gaze. The upper two channels represent movements in the vertical plane (R.V. and L.V.) and the lower two channels represent movements in the horizontal plane (R.H. and L.H.).* A four per second sinusoidal nystagmus in the vertical plane of the right eye only is shown on this record.

* This and the following records represent amplifications of the corneoretinal potential. The condenser-coupled amplifiers used record only a *change* in potential, so that if any ocular position is maintained the record will be isoelectric, deflections occurring only during movement. The slope of a deflection is roughly proportional to the velocity of the movement, so that a rapid movement in one direction, followed by a slower movement in the opposite direction (as in jerky nystagmus), appears as a saw-tooth wave (figs. 3, 5, 6, and 9). Pendular nystagmus, in which the velocity is equal in both directions, appears as sinusoidal waves (figs. 2, 4, and 7).

The four-channel electrical recording used by us was interpreted as follows:

Channel 1. Vertical movements of the right eye (R.V.). An upward deflection represents an upward movement and a downward deflection a downward movement.

Channel 2. Vertical movements of the left eye (L.V.); otherwise as in Channel 1.

Channel 3. Horizontal movements of the right eye (R.H.). An upward deflection represents a movement toward the right, and a downward deflection a movement toward the left.

Channel 4. Horizontal movements of the left eye (L.H.); otherwise as in Channel 3.

was covered, the "jumping" became most apparent. This symptom persisted and she later noted weakness, clumsiness, and tremor of the left upper extremity, followed by similar symptoms in both lower extremities. Her gait became very unsteady and she had periodic numbness of the right upper extremity.

Examination revealed a monocular nystagmus characterized by a fine, rhythmic, vertical nystagmus on direct forward and upward gazes, in the left eye only. On gaze to right or left, there was a dissociated nystagmus in the horizontal plane, with a greater amplitude in the abducted eye. On left lateral gaze the monocular nystagmus in the left eye was reduced. While the visual acuity of the right eye was normal, she could not see well with the left eye. In tests with her left eye she complained that objects were not steady. She could read headlines and subheads but not body type print with the left eye. With the right eye covered she reported (on the special test screen) a red circle and the number 5 within it, but could not identify the smaller digits around the 5. She claimed that the circle and its contents "move up and down." The optic fundi were normal. The visual fields were normal.

In addition she had a right facial paresis, decreased hearing on the right, and an intention tremor of the upper extremities, more so on the left. There was dysmetria on the heel-knee test, worse on the left. The deep tendon reflexes were hyperactive throughout. There was an equivocal right Babinski sign. Sensation was normal. The diagnosis was brainstem lesion of undetermined cause. X-ray studies of the skull and the cerebrospinal fluid were normal.

Monocular nystagmus. On direct forward and upward gazes, the electrical record of eye movements revealed sinusoidal waves at five per second in the vertical plane of the left eye only (fig. 4). This was not affected by closing the right eye or by completely darkening the room with the eyes open. When either the left eye or both eyes were closed, the nystagmus disappeared temporarily, but when she looked upward with the eyes closed, the nystagmus appeared in the left eye only. On right or left lateral gaze, the record showed a coarse, dissociated, horizontal nystagmus, most apparent in the abducted eye, suggesting what is known as the syndrome of the median longitudinal fasciculus (fig. 5). On downward gaze, the nystagmus disappeared. On convergence the five per second sinusoidal waves in the left eye were increased in amplitude.

Optokinetic stimulation produced the expected binocular nystagmus in all directions of the traveling stripes. The response to downward movements of the stripes was less than in the other planes. The spontaneous vertical monocular nystagmus could not be detected at any time during the responses to this stimulation.

Caloric stimulation (cold water) of either ear produced normal brisk binocular responses, mostly in the horizontal plane, with obliteration of the vertical monocular nystagmus in the left eye (fig. 6). When the eyes were turned away from the side of stimulation, the binocular nystagmus was very apparent as expected, but when the eyes were turned toward the side of stimulation there was no binocular nystagmus, not even the dissociated

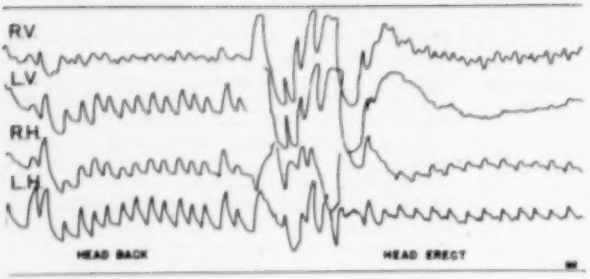

Fig. 3 (Nathanson, Bergman, and Bender). *Case 1 (B. E.).* Electrical recording of the eye movements after cold water irrigation of the left ear. With the patient looking to the right and head back, the record shows nystagmus in the horizontal and vertical planes (R.H., L.H., and L.V.) which represents the oblique characteristic of the movements. The fast component is to the right and the slow component to the left. The beat of the spontaneous vertical nystagmus of the right eye (R.V.) persisted throughout this response, and especially during the response with the head erect.

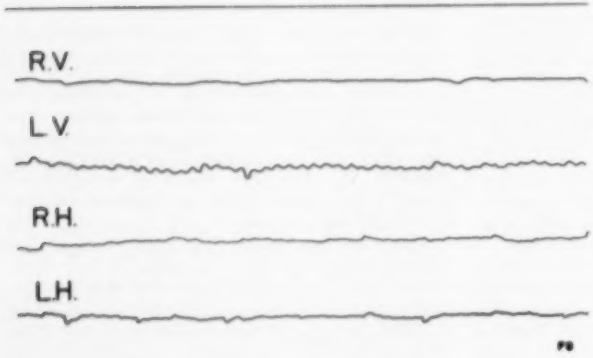

Fig. 4 (Nathanson, Bergman, and Bender). *Case 2 (F. G.).* Electrical recording with the eyes in direct forward gaze showing a five per second sinusoidal vertical nystagmus of the left eye only (L.V.).

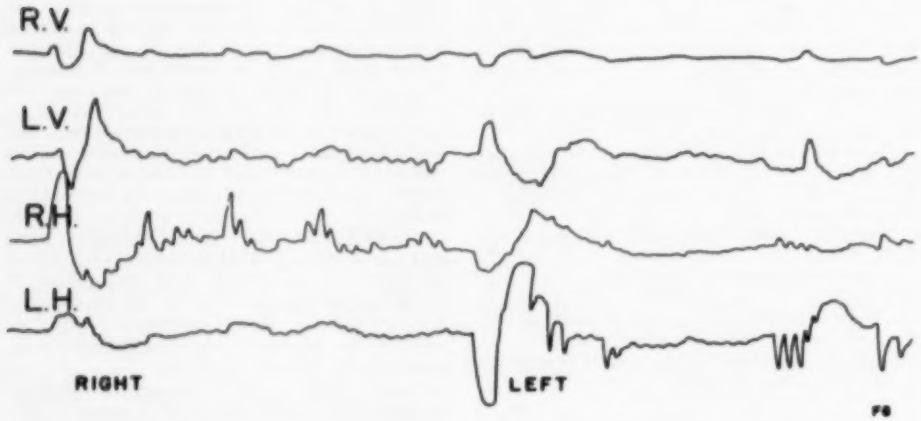

Fig. 5 (Nathanson, Bergman, and Bender). *Case 2 (F. G.).* Electrical recording of the eyes on right and left lateral gazes, showing dissociated ocular movements typical of lesions involving the median longitudinal fasciculus. Note that on right horizontal gaze the right eye abducts fully and there is barely any movement of the left eye. In addition, the right eye shows a coarse nystagmus (R.H.). On left lateral gaze (L.H.), the left eye fully abducts and shows a coarse irregular nystagmus, whereas the right eye barely moves beyond the midposition. It is of interest to note that during right lateral gaze a short run of five per second sinusoidal waves appears in the vertical plane of the left eye (L.V.) of smaller amplitude. On left lateral gaze the monocular vertical nystagmus of the left eye was not noted.

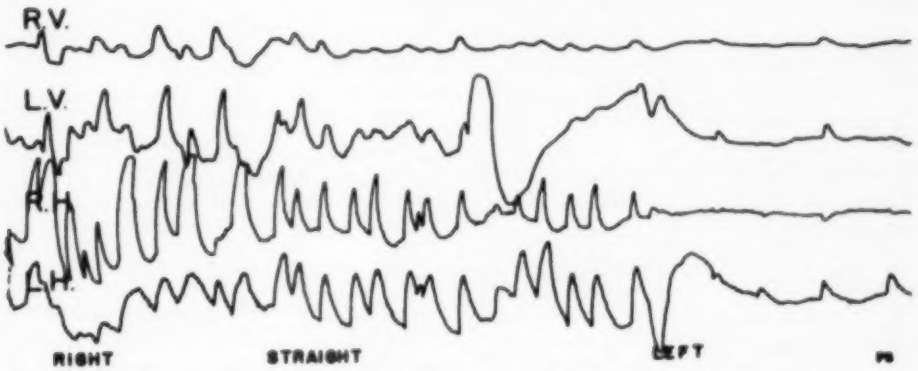

Fig. 6. (Nathanson, Bergman, and Bender). *Case 2 (F. G.).* Electrical recording of eye movements during cold caloric stimulation of the left ear showing typical nystagmus with fast and slow phases. During this response the former monocular nystagmus cannot be seen.

nystagmus on lateral gaze that existed before stimulation.

Effect of barbiturates. After receiving 100 mg. of sodium amytal intravenously in 30 seconds, the vertical monocular nystagmus in the left eye on direct forward and upward gazes disappeared. The oscillopsia in the left eye disappeared and the visual acuity was markedly improved. All digits within the red circle on the test screen were identified spontaneously with the right eye covered. She now could read body type newsprint easily. There was no scotoma. Fifteen seconds later a typical coarse, rapid, barbiturate nystagmus appeared on lateral gazes, and the dissociation of lateral eye movements became more apparent. The expected barbiturate nystagmus on upward gaze did not appear. When the effects of the drug wore off, the vertical monocular nystagmus returned.

CASE 3

This patient (M. D.), aged 36 years, had a history of exacerbations and remissions of symptoms suggesting involvement of various areas of the nervous system. The clinical impression was multiple sclerosis. She complained of "jumping of the right eye" and associated rotary oscillopsia for 12 years.

The right eye showed an oblique nystagmus with a rotary component on direct forward, lateral, and upward gazes. Objects were described as "moving round and round." She could not read subhead size print with the right eye, while the left eye was covered. On the special test screen the patient identified the red circle but the digits within the circle were referred to as "some smaller things inside the circle—maybe a five." Vision in the left eye was normal. The optic discs were reported to

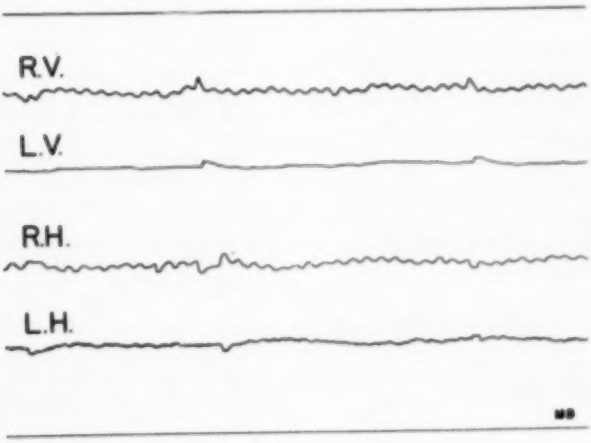

Fig. 7 (Nathanson, Bergman, and Bender). *Case 3 (M. D.).* Electrical recording of the eyes on direct forward gaze showing a five per second sinusoidal nystagmus in the vertical (R.V.) and horizontal (R.H.) planes of the right eye, representing oblique ocular movements.

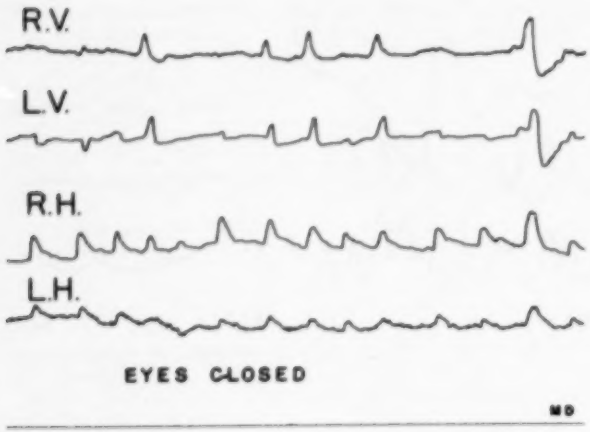

Fig. 8 (Nathanson, Bergman, and Bender). *Case 3 (M. D.)* Electrical recording of the same patient with her eyes closed showing the disappearance of the five per second nystagmus in the right eye (R.V.). The sharp deflections seen on this record represent rapid movements associated with movements of the eyelids.

show "bitemporal pallor" but there were no visual field defects.

The electrical record on direct forward gaze revealed five to six per second sinusoidal waves in both the horizontal and vertical channels of the right eye (fig. 7). With this method of recording, oblique or rotary ocular movements are picked up by horizontal and vertical channels. Total darkness failed to alter these movements, but when she closed her eyes, the nystagmus temporarily stopped (fig. 8).

Optokinetic stimulation in the horizontal directions elicited the expected binocular nystagmus. However, the record showed a *persistent*, though less regular, monocular nystagmus in the vertical plane of the right eye (R.V., fig. 9). The monocular nystagmus previously seen in the horizontal plane of the right eye (R.H., fig. 7), was obliterated by the opticomotor nystagmus. Optokinetic stimulation in the vertical directions produced the expected vertical nystagmus, but the monocular nystagmus of the right eye was seen to persist in the horizontal plane (R.H.). In other words, the rotary component of the monocular nystagmus, represented by pendular waves in the vertical and horizontal channels, persisted in either channel depending on the direction of the stripes.

Caloric stimulation of either ear induced a marked ocular response in the horizontal plane. During the height of the response, both eyes moved equally and the monocular nystagmus was no longer seen but, as the vestibular response waned,

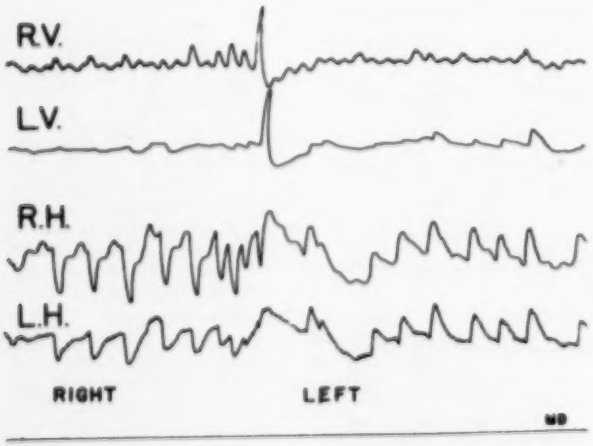

Fig. 9 (Nathanson, Bergman, and Bender). *Case 3 (M. D.)* Electrical recording of the eyes during opticomotor stimulation in the horizontal plane (R.H., L.H.). Note that despite the horizontal nystagmus the former five per second sinusoidal vertical nystagmus in the right eye persists.

the nystagmus in the right eye promptly reappeared.

Effect of barbiturates. After receiving 125 mg. of sodium amytal intravenously in 60 seconds, the monocular nystagmus of the right eye on direct forward gaze temporarily disappeared. At the same time she reported disappearance of the oscillopsia. The patient now identified correctly all the digits within the red circle and was able to read body type newsprint with few errors. Typical barbiturate nystagmus appeared in both lateral and vertical gazes.

Discussion

The foregoing observations disclose that acquired nystagmus is not always binocular. It is significant that monocular nystagmus can be abolished, at least temporarily, by intravenous injections of barbiturates and by closing of the eyes. However, total darkness, with the eyes open and in the midposition, did not affect the rate and character of the monocular nystagmus in all cases. The monocular nystagmus persisted. Since darkness does not abolish the nystagmus, it follows that the eye closure does not produce its inhibitory effect on nystagmus by exclusion of vision. The abolition of the nystagmus by eyelid closure is probably related to the upward rolling of the eye which normally occurs in eye closure.

Some of the interesting phenomena demonstrated by electrical recording were alteration and actual obliteration of monocular nystagmus and, in some instances, a failure to influence this nystagmus by the superimposed vestibular and optokinetic bilateral nystagmus. Thus, in Case 1, the vertical monocular oscillating movements were apparent in the electrical recording even when there were strong horizontal to-and-fro excursions produced by caloric stimulation. In Case 3, opticomotor stimulation in the horizontal and vertical planes failed to abolish the monocular nystagmus.

At present we have no satisfactory explanation for these findings, since, for the most part, opticomotor and caloric stimulation obliterated the monocular excursions. The findings merely suggest that the ocular responses produced by these stimuli "masked" the monocular nystagmus instead of stopping it.

Whereas most nystagmus observed clinically and by means of electrical recording shows a quick and slow component, the nystagmus on direct forward gaze herein described (either monocular or binocular) is almost always pendular in character.* Moreover, the rate is commonly four to six beats per second, whereas caloric or opticomotor nystagmus in the same patient is slower, two to three beats per second.

What we refer to as nystagmus on direct forward gaze has been termed amblyopic nystagmus by some and fixation nystagmus by others.[4] The nystagmus has been attributed to "defective central vision" or explained as "an ataxia of extraocular muscles deprived of tonic control of macular impulses." In our cases there was no evidence of central field defects and the visual acuity actually improved when the nystagmus was abolished with barbiturates. Moreover, complete darkness, where there was no question of visual acuity, failed to abolish these movements.

The anatomy of the lesion in cases of monocular nystagmus is not well known. Although binocular jerky nystagmus may be produced by lesions in the tegmentum of the brainstem and monocular dissociated horizontal nystagmus on ocular deviation by a lesion in the median longitudinal fasciculus, we have no information as to the site of lesion in cases of monocular vertical nystagmus on forward gaze.[5-7]

Binocular vertical nystagmus is known to occur as a result of an experimental lesion in both median longitudinal fasciculi of the monkey. However, we have no clear data that a lesion of one median longitudinal fasciculus will produce a monocular vertical nystagmus. Thus far we have not succeeded

* We have observed binocular nystagmus on direct forward gaze with quick and slow phases in the horizontal plane and have recorded one case with the jerky nystagmus in the horizontal plane.

in producing a lesion in only one median longitudinal fasciculus in the monkey. Moreover, clinicopathologic studies of lesions in one median longitudinal fasciculus in man make no mention of monocular vertical nystagmus.

Vague reference has been made to monocular nystagmus as a result of an incision in the midbrain or by stimulation of this area in animals.[8] Judging from their description, the anatomy of this incision is not precise and it is not clear whether the resultant nystagmus was on direct forward gaze or only when the eyes were moved away from the midposition.

From preliminary studies on monkeys we suspect that in our cases of monocular nystagmus the structural defect is located in the tegmentum of the brainstem. This might be somewhere between the level of vestibular and collicular zones, and possibly near the median longitudinal fasciculus.

Summary

1. Three cases of acquired monocular nystagmus on direct forward gaze are described and illustrated by means of electrical recording of ocular movements. In two cases, the nystagmus was in the vertical plane and in the third, in the oblique, with a rotary component.

2. The monocular nystagmus was pendular (four to six per second sinusoidal waves) in all three cases.

3. Intravenous injections of barbiturates or closing of the eyes temporarily abolished the monocular nystagmus in each case.

4. Exclusion of visual stimuli by absolute darkness failed to alter the monocular nystagmus.

5. Nystagmus induced by vestibular (caloric) and visual (opticomotor) stimulations affected the monocular nystagmus in some instances and not in others.

6. The possible anatomic sites responsible for the production of acquired monocular nystagmus are considered in light of other known anatomic lesions that produce dissociated ocular movements in man and in experimental animals.

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References

1. Duane, A.: Unilateral and other unusual forms of nystagmus. New York State J. Med., **5**:245-249, 1905.

2. Bergman, P. S., Nathanson, M., and Bender, M. B.: Electrical recording of normal and abnormal eye movements modified by drugs. Arch. Neurol. & Psychiat., **67**:357-374 (Mar.) 1952.

3. Nathanson, M., Bergman, P. S., and Bender, M. B.: Visual disturbances as the result of nystagmus on direct forward gaze: Effect of sodium amytal. Arch. Neurol. & Psychiat., **69**:427-435, 1953.

4. Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby, 1949, v. 4, pp. 4213-4214.

5. Bender, M. B., and Weinstein, E. A.: Effects of stimulation and lesion of the median longitudinal fasciculus in the monkey. Arch. Neurol. & Psychiat., **52**:106-113, (Aug.) 1944; Tr. Am. Neurol. A., 1944, pp. 184-187.

6. ———: The syndrome of the median longitudinal fasciculus. A. Res. Nerv. & Ment. Dis., **28**: 414-420 (Feb.) 1950.

7. Bender, M. B., and Bergman, P. S., and Nathanson, M.: Dissociation of ocular movements in brain stem disorders. Tr. Am. Neurol. A., 1954.

8. Arkin, W., and Sterling, W.: Le nystagmus monoculaire. Arch. d'ophtal., **43**:77-82, 1926.

THE COEFFICIENT OF OUTFLOW OF AQUEOUS*

WITH THE WATER TEST AND FOLLOWING THE USE OF DIAMOX

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The tonographic studies of Becker and Friedenwald[1] indicated that the water test usually causes an elevation of pressure and an associated induced decrease in facility of outflow (C). They found cases in which the C value was unchanged by a positive water test to be rare. deRoetth[2] found the opposite to be the usual situation. He also found that artificial changes in the osmotic pressure of the blood caused changes in the rate of aqueous flow into the eye which causes variation in the intraocular pressure. A tonographic study on three series of eyes, 30 normal, 29 with unoperated chronic simple glaucoma, and 29 with successfully operated chronic simple glaucoma, was undertaken in order to ascertain the dominant effect. The findings of deRoetth were corroborated.

A similar study was made on the same patients to determine the effect of Diamox on the coefficient of outflow. The observations were made two hours following the beginning of the water-test studies for comparison of these particular values.

METHOD

The material for this study included 30 normal eyes of 15 patients from the Eye Clinic, Receiving Hospital, Detroit—26 eyes in 15 patients with unoperated chronic simple (open-angle) glaucoma and 29 eyes of 19 patients with successfully operated simple glaucoma. The glaucoma patients were from the Glaucoma Clinic, Receiving Hospital, and a minority from private practice. The unoperated simple glaucoma patients selected had had previous elevations of tensions to between 35 and 45 mm. Hg (Schiøtz) but their tension at the time of the tests after no medication for a period of 36 hours was between 16 and 41 mm. Hg (Schiøtz, 1954 scale). The diagnosis had been based on the diagnostic criteria of chronic simple glaucoma—namely, elevated pressure and field and disc changes.

Each patient was subjected to tonography on an ambulatory basis. All tensions were taken with the Mueller electrotonometer. A voltage control was used at all times. The aqueous outflow tests were carried out for a four-minute period, according to Grant's method. The tension was measured 30 minutes before the first tonographic study in each case to consider any rising or descending phase of intraocular pressure. After the first tonographic study, the tension was measured in 30 minutes and the patient given a liter of water to drink within a five-minute period. The tension was taken in 30 minutes and a tonographic study made. A half hour later the tension was measured and 500 mg. Diamox given orally. The tension was measured one hour later and the final tonographic study made. The results of these measurements are shown in the tables. The average values are shown in Table 1.

RESULTS

WATER TEST

In the 30 normal eyes studied, the water test caused little change in the intraocular pressure—an average rise of only 1.9 mm. Hg one-half hour after the test. The facility of outflow remained the same while the rate of flow increased from 1.60 to 1.92 cu. mm. per minute.

In 26 glaucomatous eyes the ocular tension *rose* from an average of 23.68 mm. Hg to 32.42 mm. Hg in one-half hour (+8.7 mm.). The facility of outflow and resistance (R) did not change significantly but the rate of

* From the Glaucoma Clinic, Detroit Receiving Hospital.

TABLE 1

AVERAGE RESULTS OF TONOGRAPHY IN NORMAL AND GLAUCOMATOUS EYES AFTER THE WATER TEST AND USE OF DIAMOX

	No. Eyes	Control Intraocular Pressure mm. Hg (Schiøtz 1954)	Initial Intraocular Pressure (mm. Hg)	# Water			Tension 30 min. Before Water Test (mm. Hg)	Intraocular Pressure 30 min. After Water (mm. Hg)	# Water			Tension 30 min. after Tonography (mm. Hg)	Intraocular Pressure One hour after Diamox (mm. Hg)	Diamox		
				C	R	F			C	R	F			C	R	F
Normal	30	14.9	14.5	0.148	6.75	1.60	13.8	15.7	0.15	6.66	1.92	14.25	13.99	0.136	6.41	1.52
Unoperated chronic simple glaucoma	20	24.52	22.75	0.083	12.04	1.52	23.68	32.42	0.066	15.15	1.71	30.69	21.85	0.085	11.76	1.50
Successfully operated chronic simple glaucoma	20	16.25	16.08	0.152	6.58	2.19	16.05	19.03	0.15	6.66	2.30	16.14	14.36	0.135	7.40	1.52

flow *increased* from 1.52 to 1.71 cu. mm. per minute.

In 29 successfully operated eyes with chronic simple glaucoma the ocular tension rose 3.0 mm. Hg in one-half hour, the facility of outflow and resistance remained the same, while the rate of flow remained the same. It must be noted here, however, that the bleb drainage must be taken into account in evaluating the tonographic results.

Diamox

In the normal eyes Diamox caused an average decrease in tension of less than 1.0 mm. in one hour, no different than in the control. The facility of outflow and resistance remained the same and the rate of flow decreased from an average of 1.92 to 1.52 cu. mm. per minute in one hour.

In unoperated chronic simple glaucoma the ocular tension decreased 9.1 mm. in one hour. The facility of outflow increased slightly (0.66 to 0.85) in one hour (the resistance fell from 15.15 to 11.76) and the rate of flow decreased slightly from 1.71 to 1.50 cu. mm. per minute.

In operated glaucoma simplex the ocular tension decreased insignificantly in one hour from 16.1 to 14.4 mm. Hg. The facility of outflow remained the same while the rate of flow decreased from 2.30 to 1.52 cu. mm. per minute. Here the effect on the rate of flow is like that found in the normal. The filtering cicatrix must be considered as the reason for this.

Comment

The water test, as shown by deRoetth,[2] acts as does a decrease in osmotic pressure, causing an increase in ocular tension and rate of flow in normal and glaucomatous eyes. An increase in facility of outflow is found only in normal eyes. No change occurs in glaucoma. There is a slight increase in ocular tension in normal eyes and a considerable increase in eyes with simple glaucoma. Our findings corroborate deRoetth's observations.

Diamox caused no significant change in

TABLE 2

RESULTS OF TONOGRAPHY IN NORMAL EYES

Eye No.	Control (mm. Hg Schiötz)	First Tonography			Control 30 min. after after Tonographing (mm. Hg)	Water			Control 30 min. after Water Test	Diamox		
		Initial Tension (mm. Hg)	C	F		Initial Tension mm. Hg 30 min. after Water	C	F		Initial Tension One hr. after Diamox	C	F
1	20.0	21.9	0.18	3.23	18.8	26.4	0.20	4.89	20.0	18.8	0.17	2.6
2	19.4	18.8	0.12	1.78	18.8	24.0	0.11	2.2	18.2	18.5	0.18	2.6
3	12.8	12.8	0.14	1.24	9.6	11.1	0.09	0.64	11.7	11.4	0.10	0.75
4	10.2	8.6	0.08	0.37	7.9	12.3	0.12	0.10	9.6	10.2	0.09	0.56
5	13.6	10.1	0.12	0.76		14.0	0.17	1.77	13.6	13.4	0.27	2.54
6	11.8	9.9	0.12	0.74		11.4	0.08	0.59	12.5	11.3	0.13	0.99
7	15.7	16.2	0.12	1.53		19.4	0.20	3.1	16.48	16.72	0.12	1.59
8	16.25	16.2	0.16	1.96		16.7	0.16	2.0	16.01	14.82	0.12	1.30
9	17.6	18.8	0.16	2.38	14.4	18.8	0.10	1.89	17.2	16.2	0.14	1.71
10	17.2	16.7	0.12	1.53	13.6	17.6	0.12	1.70	17.6	14.0	0.125	1.26
11	14.8	13.2	0.11	1.02	13.0	14.4	0.12	1.25	14.0	12.5	0.08	0.68
12	14.8	11.4	0.10	1.15	11.9	14.0	0.10	1.4	12.8	10.25	0.08	0.53
13	15.3	16.7	0.10	1.27	14.8	17.2	0.06	0.79	18.3	14.8	0.12	1.35
14	12.8	11.4	0.05	0.37	12.5	12.8	0.06	0.53	12.8	12.8	0.14	1.24
15	17.2	16.6	0.30	3.8	12.5	16.25	0.18	2.2	14.4	14.8	0.30	3.24
16	16.6	15.7	0.21	2.4	14.0	15.3	0.26	2.94	13.6	12.8	0.17	1.51
17	11.8	11.4	0.12	0.90	11.9	13.2	0.15	1.38	12.5	10.5	0.16	1.04
18	11.15	11.15	0.175	1.25	9.6	11.4	0.14	1.05	10.5	8.6	0.12	0.55
19	17.23	14.8	0.15	1.62	15.3	20.0	0.30	4.81	14.8	13.6	0.23	2.22
20	15.3	14.8	0.125	1.35	14.0	18.2	0.18	2.66	13.64	11.15	0.14	1.0
21	17.66	17.6	0.21	2.87	14.8	14.0	0.14	1.40	14.0	14.8	0.14	1.51
22	14.4	13.8	0.20	1.97	14.8	11.1	0.12	0.89	13.6	12.8	0.18	1.59
23	14.4	14.0	0.15	1.5	14.4	14.8	0.18	1.96	13.6	13.6	0.11	1.06
24	10.3	10.2	0.10	0.62	12.1	11.8	0.13	1.0	11.4	12.1	0.10	0.82
25	14.8	16.2	0.18	2.2	16.6	20.0	0.21	3.37	16.01	14.8	0.28	3.03
26	15.30	16.2	0.14	1.72	16.0	17.2	0.15	1.98	14.8	11.97	0.15	1.20
27	14.4	14.0	0.13	1.30	15.7	15.3	0.15	1.70	15.2	13.6	0.15	1.45
28	12.87	12.8	0.10	0.88	15.3	13.2	0.11	1.02	13.6	15.2	0.15	1.38
29	18.2	18.2	0.30	4.27	17.6	17.6	0.30	4.1	14.4	14.4	0.25	2.60
30	16.01	16.25	0.17	2.08	14.4	13.6	0.18	1.7	12.8	13.4	0.20	1.89

TABLE 3

RESULTS OF TONOGRAPHY IN UNOPERATED SIMPLE GLAUCOMA

Eye No.	Control (mm. Hg Schiötz)	First Tonography			Control 30 min. after Tonography (mm. Hg)	Water			Control 30 min. after Water Test	Diamox		
		Initial Tension (mm. Hg)	C	F		Initial Tension mm. Hg 30 min. after Water	C	F		Initial Tension One hr. after Diamox	C	F
1	33.75	23.1	0.05	0.95		50.6	0.02	0.92	55.3	33.7	0.03	0.89
2	27.3	20.0	0.025	0.40		33.7	0.02	0.60	34.7	24.4	0.02	0.41
3	24.8	22.0	0.025	0.45	22.6	34.5	0.04	1.22	24.8	21.6	0.01	0.14
4	21.3	18.2	0.04	0.57	19.4	24.0	0.04	0.80	21.2	14.8	0.01	0.11
5	18.5	18.5	0.15	2.1	18.5	22.6	0.19	3.53				
6	23.1	24.0	0.03	0.72	23.11	33.2	0.02	0.58				
7	18.8	16.9	0.13	1.68		33.1	0.035	1.01	36.7	27.3	0.11	2.56
8	28.2	28.2	0.12	2.91		34.3	0.02	0.61	36.7	22.5	0.08	1.46
9	18.2	14.8	0.06	0.65		25.6	0.08	1.73	20.3	19.4	0.22	3.40
10	17.7	17.7	0.15	2.01	17.7	23.1	0.14	2.68	21.3	14.8	0.125	1.35
11	18.2	17.2	0.08	1.06	17.7	20.0	0.07	1.20	21.3	15.3	0.08	0.90
12	24.8	28.67	0.05	1.23	30.9	41.6	0.03	1.13	51.06	26.76	0.05	1.14
13	21.29	25.23	0.01	0.21	29.1	38.0	0.01	0.34	40.4	21.6	0.02	0.35
14	27.3	27.3	0.10	2.43	24.8	36.7	0.02	0.82	33.7	24.5	0.06	1.23
15	24.0	22.6	0.06	1.12	23.1	34.9	0.03	0.93	32.3	21.0	0.04	0.77
16	33.7	29.1	0.06	1.51	26.0	31.8	0.07	1.95	30.0	19.0	0.04	0.60
17	26.01	21.3	0.03	0.52	20.1	28.3	0.05	1.22	22.5	14.8	0.035	0.38
18	26.0	28.3	0.10	2.43	27.5	33.7	0.08	2.38	31.8	23.2	0.12	2.30
19	30.0	30.0	0.04	1.06	32.8	41.6	0.04	1.51	38.06	23.8	0.095	1.89
20	25.2	21.3	0.10	1.73	20.5	35.5	0.12	3.78	27.3	20.5	0.08	1.32
21	16.0	14.4	0.12	1.25	14.0	18.2	0.09	1.28	17.2	12.8	0.07	0.62
22	19.4	20.0	0.21	3.36					21.9	17.2	0.16	2.11
23	16.2	17.6	0.20	2.73	15.7	18.2	0.15	2.14	19.4	20.6	0.23	3.83
24	34.7	34.7	0.08	2.46	36.8	48.7	0.09	4.02	32.8	28.3	0.09	2.19
25	36.4	36.4	0.09	2.79	27.1	35.0	0.17	5.1	24.2	22.4	0.10	1.91
26	26.3	26.0	0.06	1.31	26.3	33.6	0.05	1.43	37.0	26.4	0.19	4.29

TABLE 4

RESULTS OF TONOGRAPHY IN SUCCESSFULLY OPERATED GLAUCOMATOUS EYES

Eye No.	Operation	Control (mm. Hg Schiötz)	First Tonography			Control 30 min. after Tonography (mm. Hg)	Water			Control 30 min. after Water Test	Diamox		
			Initial Tension (mm. Hg)	C	F		Tension mm. Hg 30 min. after Water Initial	C	F		Initial Tension One hr. after Diamox	C	F
1	cyclo.	6.6	6.2	0.19	1.38	5.0	9.4	0.15	1.40	11.9	10.0	0.20	1.93
2	trephine	19.0	17.0	0.07	1.04	18.8	28.5	0.08	1.92	29.6	19.0	0.04	0.65
3	trephine	18.6	21.8	0.38	7.05	22.2	24.6	0.49	10.2	16.9	16.9	0.34	5.03
4	trephine	26.5	27.1	0.32	7.39	26.5	28.1	0.39	9.37	22.8	22.8	0.16	1.65
5	trephine	13.2	16.0	0.16	2.24	13.8	14.2	0.13	2.16	14.8	13.4	0.20	2.43
6	trephine	14.0	16.6	0.21	3.01	12.5	16.9	0.22	3.2	15.0	13.7	0.24	2.98
7	trephine	11.9	10.6	0.15	1.50	7.5	11.7	0.21	2.31	10.2	10.2	0.18	1.76
8	trephine	9.6	11.5	0.42	4.55	11.9	10.4	0.14	1.31	8.8	9.2	0.26	2.37
9	trephine	25.7	25.7	0.15	3.29	22.8	29.0	0.17	4.22	20.7	24.8	0.16	3.40
10	trephine	11.8	10.6	0.04	4.0	10.6	11.0	0.02	0.21	10.0	10.4	0.09	0.89
11	trephine	29.0	25.7	0.14	3.07	24.0	35.8	0.17	5.2	31.0	23.4	0.16	3.20
12	trephine	20.1	16.3	0.07	1.0	16.0	22.0	0.09	1.72	21.0	12.5	0.05	0.56
13	iridenel.	11.2	13.2	0.18	1.70		13.2	0.15	1.38		8.39	0.14	0.61
14	trephine	16.5	19.15	0.07	1.13		25.0	0.08	1.68		16.1	0.075	0.91
15	trephine	16.7	16.7	0.11	1.40		18.2	0.12	1.7		14.8	0.095	1.03
16	trephine	15.2	16.1	0.07	0.91		17.9	0.11	1.53		13.9	0.04	0.39
17	trephine	15.0	14.0	0.175	1.75		16.0	0.17	2.1		12.9	0.20	1.8
18	trephine	17.7	17.9	0.09	1.26		20.00	0.12	1.96		17.5	0.20	2.7
19	trephine	17.6	17.6	0.15	2.04		16.5	0.10	1.25		17.23	0.09	1.19
20	trephine	17.6	18.7	0.10	1.47		18.7	0.08	1.17		16.5	0.08	1.0
21	iridenel.	22.6	25.0	0.14	2.94		24.0	0.08	1.6		16.1	0.05	0.61
22	iridenel.	25.0	20.65	0.08	1.41		19.7	1.5	0.59		17.6	0.02	0.34
23	trephine	11.4	9.9	0.17	1.04		12.1	0.15	1.21		11.4	0.15	1.11
24	iridenel.	11.4	11.4	0.17	1.26		11.9	0.16	1.27		10.2	0.17	1.06
25	iridenel.	15.7	15.7	0.16	1.88		15.5	0.11	1.27		12.1	0.20	1.62
26	iridenel.	7.5	6.9	0.04	0.12		7.6	0.07	0.25		7.0	0.01	0.03
27	trephine	10.5	9.8	0.20	1.16		12.30	0.27	2.30	9.8	9.8	0.14	0.85
28	iridenel.	17.9	18.5	0.13	1.89	20.6	18.5	0.13	1.89	17.6	17.6	0.10	1.36
29	iridenel.	11.8	10.2	0.10	0.62	12.5	11.15	0.06	0.43	11.1	11.15	0.11	0.79

ocular tension or the facility of outflow in normal eyes. In unoperated eyes with simple glaucoma, Diamox caused an average decrease in ocular tension of 9.1 mm. in one hour and a decrease in resistance to outflow. In successfully operated eyes with simple glaucoma there was an average decrease in ocular tension of 4.5 mm. in one hour. The resistance to outflow was unchanged.

In all three series of eyes Diamox caused a decrease in rate of flow. In normal eyes the average rate fell from 1.92 to 1.52 cu. mm. per minute. In unoperated eyes with simple glaucoma, the average rate of flow decreased from 1.71 to 1.50 cu. mm. per minute and in successfully operated eyes with simple glaucoma the average rate fell from 2.30 to 1.52 cu. mm. per minute. The average rate of flow after Diamox was the same in the three series.

In these cases the most significant difference between the water test and the effect of Diamox was in the rate of flow. In normal, unoperated, and operated eyes with glaucoma simplex the water test increased the flow rate significantly while Diamox caused the opposite effect.

Friedenwald and Becker[1] pointed out the variation in results of tonography from one eye to the next due to various sources of error including the changes in blood volume due to fright or emotional vascular change, change in the diastolic blood pressure at the beginning of tonography, and changes in scleral rigidity. One should not attach undue importance to the absolute values obtained with tonography when comparing one eye with another or when comparing the readings with the previously established normal values. However, when done on the same eye at intervals the relative values may be significant.

In these studies no attempt was made to wait four to five minutes between tonographic studies on the two eyes of the same patient to avoid the spontaneous effect of one eye in lowering the tension of the other as pointed out by deRoetth.[2]

In evaluating the usefulness of tonography in individual patients, especially in diagnosis

of early chronic simple glaucoma, Stepanik[3] found that in every eye with simple glaucoma the resistance values were normal at some portion of the diurnal curve. The highest values of resistance corresponded to the peak of the diurnal curve. Thus the diagnosis of glaucoma simplex can only be excluded if the resistance is found to be normal at the time of the peak of the diurnal pressure curve. This would require determination of the diurnal curve in each case. Horwich and Breinin[4] found that the rising phase of the diurnal curve is usually accompanied by a decreased facility of outflow.

The findings of Stepanik[3] and Horwich and Breinin[4] do not agree with those of de-Roetth who found the resistance to outflow to be uninfluenced by diurnal changes in aqueous-humor dynamics.

All of these studies point to the fact that tonography should be only a part of glaucoma diagnosis and treatment and should not be considered the salient diagnostic feature. There are so many variables that tonography must be used with caution. It would certainly be folly to consider surgery necessary on the basis of a single tonographic study if all other criteria were not present.

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REFERENCES

1. Becker, B., and Friedenwald, J. S.: Clinical aqueous outflow. Arch. Ophth., **50**:557, 1953.
2. deRoetth, A., Jr.: Effect of change in osmotic pressure of blood in aqueous humor dynamics. Arch. Ophth., **52**:571, 1954.
deRoetth, A., Jr., and Knighton, W. S.: Clinical evaluation of the aqueous flow test: A preliminary report. Arch. Ophth., **48**:148, 1952.
de Roetth, A., Jr.: Relation of tonography to phasic variations in intraocular pressure. Arch. Ophth., **51**:740, 1954.
3. Stepanik, J.: Diurnal tonographic variations and their relation to visible aqueous outflow. Am. J. Ophth., **38**:429, 1954.
4. Horwich, H., and Breinin, G. M.: Phasic variations in tonography. Arch. Ophth., **51**:687, 1954.

TOPICAL ANESTHESIA IN OPHTHALMOLOGY*

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This study was stimulated by a recent report of several new synthetic anesthetics that possess an action far more potent than those in common use today, without a corresponding increase in toxicity.[1] Most previous studies of topical anesthetics have considered only a few of the characteristics of the anesthetics studied. In almost every study, the methods of evaluation selected have been different. Before proceeding with our experiments, we found it necessary to consider what characteristics are desirable in an anesthetic to be used in the eye.

IDEAL TOPICAL ANESTHETIC FOR THE EYE

Any anesthetic to be used in the eye must meet more rigid requirements than necessary for topical use anywhere else in the body. The characteristics desirable may vary

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slightly with the ocular procedure to be performed. It is preferable to select a single anesthetic drug most satisfactory for all uses than to resort to different drugs for different purposes.

I. Anesthetic potency

The potency of any anesthetic is influenced by many factors. The anesthesia produced by a subcutaneous injection may not in any way be similar to that obtained after instillation in the eye. Swan and White[2] have shown this apparent discrepancy to be the result of a variability in corneal permeability. They have found this variability to be related to "the molecular structure and the resultant physical properties of the drug," as well as the physical properties of the vehicle. Therefore, the potency of the drug when used in the eye is related in part to the true anesthetic potency and in part to the ability of the drug to penetrate the cornea and conjunctiva.

A. *Rapidity of action.* It is desirable that the anesthetic produce anesthesia of sufficient depth for the usual procedures of a minor nature, such as tonometry, within a few seconds. Deeper anesthesia, as for major ocular surgery, should be obtained in a few minutes.

B. *Depth of anesthesia.* The depth of anesthesia required varies with the procedure. The proper instillation of one drop of the drug should be sufficient to permit tonometry. The instillation of three to four drops at intervals should produce anesthesia of sufficient depth to permit major ocular surgery. The depth of anesthesia is dependent on good penetration. The penetration of the cornea by the drug is not necessarily the same as of the conjunctiva. In a congested eye it is difficult to anesthetize the conjunctiva with topical instillations. The ideal anesthetic would anesthetize cornea and conjunctiva equally well in all instances.

C. *Duration of anesthesia.* Since the length of time required to perform the various procedures on the eye varies to a great degree, it is difficult to determine what would be the ideal duration of anesthesia.

It is probably chiefly for this reason that Schlegel and Swan[3] have stated: "It seems unlikely that there can be a single local anesthetic agent superior to others for all phases of ophthalmologic practice."

We feel that the duration as well as depth of anesthesia may be altered sufficiently in most cases by merely changing the dosage. Light anesthesia from a single instillation should last no longer than 10 to 15 minutes. Deeper anesthesia from multiple instillations should last at least 45 minutes.

II. Secondary ocular effects

A. *Effect on the corneal epithelium.* One of the major objections to many drugs available for ocular anesthesia is the toxic effect on the corneal epithelium. This effect was considered by Gundersen and Liebman in their evaluation of topical anesthetics.[4] They compared the inhibitory effect of several topically instilled anesthetics on the regeneration of the epithelium following a corneal abrasion. This effect was also noted by Smelser and Ozanics[5] who observed an inhibition of mitosis and cell division in the corneal epithelium.

Edema of the epithelium may be observed following too frequent instillations of most topical anesthetics known today and at times has interfered with gonioscopy. On other occasions a loss of epithelium has been seen in the operating room when too frequent instillations of the drug have been made. These effects are well known to all ophthalmologists and occur with any of the topical anesthetics used today.

It is to be hoped that a topical anesthetic can be found that has no toxic effect on the corneal epithelium.

B. *Effect on pupil size and tension.* The frequent use of topical anesthetics for tonometry in glaucomatous and nonglaucomatous eyes is the chief reason a drug is desired that will neither affect pupil size nor the tension. Cocaine has so far been the only topical anesthetic which affects the pupil.

C. *Pain and irritation.* It is desirable that

the patient does not experience any pain or discomfort when the drug is instilled in the eye. It is even more important that no ocular congestion or irritation results from the instillation. Any resulting irritation is to a certain extent an indication of a toxic effect.

Dietrich and Beutner[6] considered the irritation from topical instillations of anesthetics to be of great importance in rating them. In deciding on the relative value of anesthetics they determined the minimal anesthetic concentration[7] and the maximal nonirritating concentration for each. Their work would have been more valuable if human subjects had been used instead of rabbits.

The ideal anesthetic certainly would cause no congestion of the eye when used topically.

III. Systemic effects

A. *Allergenicity*. All anesthetics used in ophthalmology at the present time occasionally cause an allergic reaction. In spite of the similarity of chemical structures, once an allergy has developed to one of the anesthetics another product can safely be used. A drug that is nonallergenic would be desirable.

B. *Shock*. The occasional occurrence of shock and collapse following the topical administration of cocaine is well known. A similar reaction has been reported following the topical use of tetracaine in the nose.[8] We have observed collapse in a patient on whom a two-percent tetracaine solution was used to anesthetize the nasolacrimal duct prior to probing. The ideal anesthetic should be free from such reactions in any concentration that might be commonly used in clinical practice.

C. *Addiction*. An anesthetic drug must not be habit forming. The prominent location of these drugs in most offices and clinics creates a problem if addiction can occur. At the present time cocaine is the only drug of this group that causes addiction.

IV. Chemical characteristics in solution

In addition to those chemical characteristics of the drug which govern its anesthetic action and penetration of ocular tissues, other characteristics are important.

A. *Stability*. The drug must be stable in solution for long periods of time without loss of potency. It is also advantageous if the solution can be boiled without deterioration.

B. *Sterility*. It is not sufficient that a sterile and stable solution can be prepared. The routine use of a topical anesthetic in an ophthalmologic office or clinic frequently results in contamination of the solution. It is therefore desirable that the solution have self-sterilizing qualities. It is not necessary that this germicidal quality be inherent in the anesthetic itself. Another agent may be added to the solution as long as it does not effect the potency or stability of the anesthetic.

Methods of evaluation

In evaluating the usefulness of any new topical anesthetic one should compare its characteristics with those of one or more of the anesthetics in common use today. The chemical characteristics should be known before clinical studies are begun. If the chemical characteristics are not satisfactory, it is useless to proceed further.

A determination of the relative anesthetic potency should be the first consideration. Many factors such as dosage, solubility, and toxicity will influence potency studies. For comparative purposes one may consider the potency of a dose for each drug just under the toxic level. Potency cannot be considered without a simultaneous consideration of toxicity. Many times it is preferable to use a concentration of the drug found useful on clinical trial.

In measuring the anesthesia produced with topical instillations several methods have been used. Several investigators have tested corneal anesthesia with a wisp of cotton.[9, 10] This records only tactile sensation and gives no indication of the depth of anesthesia. Bellows performed quantitative studies of

anesthetic potency using calibrated von Frey hairs.[11] His study involved both tactile and pain sensation as well as depth of anesthesia. Scheie has tested the depth of anesthesia by grasping the conjunctiva with a forceps.[12] This method would be useful as a supplement to the studies on the cornea as performed by Bellows.

Penetration studies as performed by Schlegel and Swan[3] are helpful in determining the reason for the depth of anesthesia noted in potency studies. In their experiments they unfortunately did not compare a surface anesthetic commonly used by ophthalmologists with their anesthetic.

Once the potency of the anesthetic has been determined one may proceed with toxicity studies. Gundersen and Liebman determined specifically the inhibition of epithelial regeneration.[4] They abraded the cornea of a guinea pig and then instilled each anesthetic agent in the eye every hour noting the effect on the corneal healing as determined by staining with fluorescein. This method is excellent. Smelser and Ozanics[5] used a different method to obtain similar information.

Other characteristics of the anesthetics can only be learned after prolonged clinical use. Simple clinical reports such as have been published[13, 14] have value in confirming the effects noted experimentally and recording any toxic reactions not known before. They are not of much value unless the number of cases is large.

Experimental studies

In these experiments we have attempted to determine some of the characteristics of three new topical anesthetic drugs. The methods used were very similar to those described by Bellows. One drop of the agent to be tested was instilled in the right eye of each human subject and one drop of 0.5-percent tetracaine hydrochloride was instilled in the left eye to serve as a control. Identical droppers were used for each agent so that the same quantity would be instilled.

The eyelids were held open for a short period after instillation of the drops to prevent expression of the anesthetic solution. Time was noted with a stop watch. Pupil size was recorded just prior to instilling the anesthetic solution and again after one hour. Any sensation from instillation of the drug was recorded. Conjunctival hyperemia was noted after five and 10 minutes.

The anesthesia resulting from this single instillation was tested by a series of calibrated esthesiometers similar to the von Frey hairs used by Bellows. Instead of hairs, 3-0, 4-0, and 5-0 nylon sutures were used. A segment of suture was cemented to an applicator stick at an angle of 145 degrees. This esthesiometer was then calibrated by means of an analytic balance. The amount of weight on one scale required just to bend the suture when applied perpendicularly to the other scale was taken as the calibration. This figure varies with the length of a suture as well as its thickness.

A series of esthesiometers were prepared by this method and recorded at from 0.1 gm. to 10.0 gm. After the first few experiments the 10.0-gm. esthesiometer was discarded because the stimulus was so strong that a corneal abrasion always resulted even with only a single application.

Using these esthesiometers, the corneal sensation was tested beginning 30 seconds after instillation of the anesthetic. Recordings were made at 30-second intervals for two minutes and at one-minute intervals thereafter until anesthesia had ceased.

The esthesiometer was applied perpendicularly to the corneal surface at the center of the cornea and near the limbus at the 9-o'clock position. If the response was questionable a third application was made near the limbus at the 3-o'clock position. At least two sites were chosen because corneal sensitivity varies as one approaches the center of the cornea from the limbus, and the recovery from anesthesia varies as to location. The figure selected in our calculations was for that site of the cornea showing the greatest sensitivity or least anesthesia at each time interval.

The presence of the corneal reflex was

taken to be objective evidence of absence of anesthesia. The patients were also frequently questioned as to ocular discomfort in corroboration of the state of anesthesia.

Results

Tetracaine

Tetracaine hydrochloride in an 0.5-percent solution has become by far the most frequently used anesthetic on this continent. It had been shown in studies performed in the past to be as good or better in most ways than other topical anesthetics available at the time.

TETRACAINE

Tetracaine is freely soluble in water and has a pH of 7.0 in solution. Benzalkonium chloride may be added to the solution without affecting the potency. The structural formula reveals it to be similar to procaine.

The principal objections to tetracaine are: (1) Toxicity for the corneal epithelium; (2) stinging sensation following instillation; (3) development of allergic reactions.

Sympocaine®

A new drug which represents only a slight difference of chemical structure from tetracaine is Sympocaine.® Preliminary clinical trials revealed that the use of Sympocaine hydrochloride® in an 0.5-percent solution was satisfactory.

SYMPOCAINE

Sympocaine® is normally acidic in solution but the pH can be adjusted by means of n/10 sodium hydroxide without altering the potency or causing a precipitate to form.

Fifteen human subjects were used in evaluating Sympocaine.® Seven of these persons had no undesirable sensation from the instillation of one drop of the solution. On the other hand, only two of them failed to complain of a stinging sensation from the tetracaine solution. The stinging sensation when it occurred was always more severe after tetracaine.

The conjunctival reaction from Sympocaine® seemed to be a little less severe than tetracaine but the difference was not significant.

No significant change in ocular tension or pupil size was noted from either drug.

The duration of action and depth of anesthesia (fig. 1) was very nearly the same for the two drugs. The slight superiority of tetracaine in this experiment was not considered sufficient to be significant.

The initial test for anesthesia following the topical instillation was made 30 seconds after the instillation. Some anesthetic effect was noted in all experiments at this time. We did not feel that we had a method reliable enough to determine the exact time of onset of the anesthesia. If there was a great difference in rapidity of action, it would have appeared evident in these experiments but minor differences go unnoticed. No difference in rapidity of action was recorded.

Ophthaine®

The standard solution of Ophthaine® in an 0.5-percent concentration as prepared by the manufacturer and recommended by Boo-

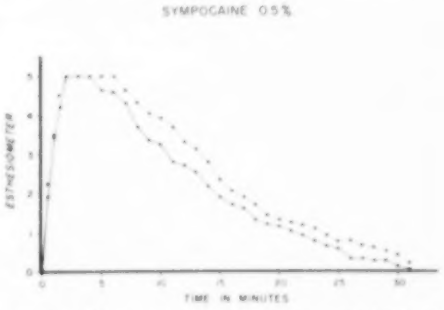


Fig. 1 (Linn and Vey). Duration and depth of anesthesia of Sympocaine hydrochloride (0.5 percent) as calibrated in gm. Abscissa = time. Ordinate = Esthesiometer. Solid line = Sympocaine. Dotted line = tetracaine (0.5 percent). The figure plotted represents the esthesiometer not felt by the patient and not causing any blinking.

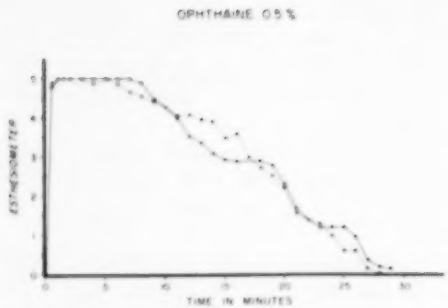
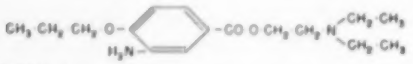


Fig. 2 (Linn and Vey). Anesthesia from Ophthaine® (0.5 percent). Solid line = Ophthaine (0.5 percent). Dotted line = tetracaine (0.5 percent).

zan and Cohen[9] was used. The similarity of chemical structure to tetracaine is again evident.



OPHTHAINE

Ophthaine® is a hydrochloride salt which is freely soluble in water and is acid in solution. The practicability of a self-sterilizing combination with benzalkonium has not been determined.

Ten human subjects were used in evaluating Ophthaine.® In this group, four persons had no unpleasant sensation from Ophthaine,® and all had a stinging or burning sensation from tetracaine. The unpleasant sensation was always worse when tetracaine was instilled.

The conjunctival reaction from Ophthaine® was always as severe as for tetracaine and in two patients was more severe.

No significant change in pupil size or tension was noted.

The duration and depth of anesthesia from Ophthaine® was about the same as tetracaine (fig. 2). Ophthaine® has been reported as having a more rapid action and shorter duration of action than tetracaine.[10] Our experiments minimize any differences.

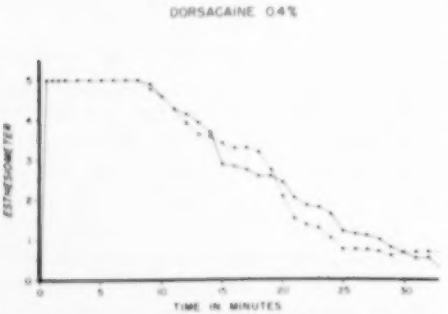


Fig. 3 (Linn and Vey). Anesthesia from benoxinate (Dorsacaine®) (0.4 percent). Solid line = benoxinate (0.4 percent). Dotted line = tetracaine (0.5 percent).

Benoxinate (Dorsacaine®)

The concentration of benoxinate of 0.4-percent solution as furnished by the manufacturer and recommended by Schlegel and Swan[3] was used.

BENOXINATE (DORSACAINE)

The structural formula of benoxinate again reveals the great similarity of structure of all of these drugs. Benoxinate is also freely soluble in water and Schlegel and Swan feel the solution has some germicidal qualities of importance in self-sterilization.

Ten patients were used in this study. Four of these persons had no sensation following instillation of the benoxinate solution but the same number had no sensation from tetracaine. The stinging sensation was equally severe no matter which drug was used.

In two patients, there was less conjunctival reaction from benoxinate. The reaction was indistinguishable in the others.

The duration and depth of anesthesia was about the same for benoxinate and tetracaine (fig. 3).

The anesthesia noted following topical instillation of one drop of all of these drugs was about the same. These experiments do not support any previous studies that report superiority of anesthetic action of one or the other of these drugs.

Clinical studies

Each one of these anesthetics has been used clinically for tonometry, removal of foreign bodies embedded in the cornea, irrigation of the lacrimal sac, and for minor surgery of the globe or conjunctiva. Satisfactory anesthesia was obtained for every purpose with each anesthetic. We were unable to notice any definite superiority of any of these drugs during the period of clinical trial.

In the routine use of these topical anesthetics for tonometry, we compared the stinging sensation on instillation and the anesthesia obtained. Each of the patients had two drops of the anesthetic instilled in each eye a few minutes apart. The new drug was always put in the right eye and tetracaine was put in the left eye. Each patient was asked if he had any sensation when the first drop was instilled. The anesthesia was considered inadequate if an additional drop had to be instilled for accurate tonometry.

The results are tabulated in Table 1. A weak dilution of Sympocaine® and a solution of Ravocaine® were also included in this study. It is noteworthy that tetracaine causes more discomfort on instillation than any of the drugs tested. The anesthesia produced by Sympocaine® (0.5 percent) Ophthaine® (0.5 percent), and benoxinate (0.4 percent) was about the same as tetracaine (0.5 percent).

No allergic response resulted in any of these patients. In two patients who were allergic to tetracaine, we used butacaine sulfate (1.0 percent) in the control eye.

Comment

It was our intention at the beginning of this investigation to obtain relative figures on topical anesthetics that would leave no doubt as to the superiority of one over all the others. Studies have been made and reported that suggest Ophthaine® and benoxinate may be more potent topical anesthetics than tetracaine.[10, 3] The results of this study indicate that any difference in potency is so small in degree that it has no significance in clinical usage of the drug.

Schlegel and Swan felt that one of the great advantages of benoxinate over tetracaine is the smaller number of allergic responses resulting from benoxinate. There is so little difference in the chemical structure of benoxinate from that of tetracaine that it is reasonable to expect allergic response to benoxinate to increase in frequency if it is used more extensively.

Actually, the chemical structures of all the drugs in this group are very similar and there is no reason to believe that one of them is more likely to produce an allergic response

TABLE 1

Anesthesia for tonometry

Anesthetic	No. Cases	Stinging Sensation after Instillation		Inadequate Anesthesia	
		New Drug	Tetracaine	New Drug	Tetracaine
Sympocaine® 0.25%	377	35 (9.2%)	125 (33.1%)	42 (11.1%)	8 (2.1%)
Sympocaine® 0.5%	204	16 (7.8%)	43 (21%)	1 (.49%)	None
Ophthaine® 0.5%	113	12 (10.6%)	36 (31%)	None	None
Dorsacaine® 0.5%	168	18 (10.7%)	66 (39.2%)	None	None
Ravocaine® 0.5%	143	16 (11.1%)	76 (53.1%)	13 (9.2%)	3 (2.1%)

than another. It is surprising that a patient can be allergic to one of them without being allergic to all of the others.

The rapidity of action of these drugs was not tested. We feel that there were great margins of error in testing the onset of anesthesia. Not much difference in the time required for anesthesia was observed when these drugs were used for various ophthalmic procedures.

Summary and Conclusions

1. The characteristics desirable in a topical anesthetic for ophthalmic procedures have been discussed.

2. A study of the depth and duration of anesthesia following ocular instillation of one drop of three new anesthetics was made. Sympocaine,® Ophthaine,® and benoxinate (Dorsacaine®) were compared with tetracaine in each experiment and were found to be equal in potency to tetracaine in the concentration used.

3. The use of each anesthetic in routine tonometry confirmed the experimental studies as to potency. Patients generally complained more of discomfort from tetracaine than any of the other three drugs. All drugs were satisfactory for all ophthalmic procedures in which topical anesthesia is used.

4. Sympocaine,® Ophthaine,® and benoxinate (Dorsacaine®) have anesthetic qualities very similar to tetracaine. They are equal but not superior to tetracaine for ocular anesthesia.

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We wish to express our sincere appreciation of the assistance given us by Mrs. Luella M. Davis who was most helpful in the clinical studies.

References

1. Luduena, F. P., Clinton, R. O., and Laskowski, S. C.: A new series of highly active local anesthetics: Science, **118**:138 (July) 1953.
2. Swan, K. C., and White, N. G.: Corneal permeability: Part I. Am. J. Ophth., **25**:1043-1057 (Sept.) 1942.
3. Schlegel, H. E., Jr., and Swan, K. C.: Benoxinate (Dorsacaine®) for rapid corneal anesthesia. Arch. Ophth., **51**:663-669 (May) 1954.
4. Gundersen, T., and Liebman, S. D.: Effect of local anesthetics on regeneration of corneal epithelium. Arch. Ophth., **31**:29-33, 1944.
5. Smelser, G. K., and Ozanics, V.: Effect of local anesthetics on cell division and migration following thermal burns of the cornea. Arch. Ophth., **34**:271-277 (Oct.) 1945.
6. Dietrich, W. C., and Beutner, R.: A search for the least irritant topical anesthetic. Anesthesiology, **7**:255-259 (May) 1946.
7. Beutner, R., and Calesnick, B.: The essential characteristics of local anesthetics. Anesthesiology, **3**: 673-682, 1942.
8. Holt, T.: A grave reaction to locally applied tetracaine hydrochloride. Arch. Otol., **42**:280, 1945.
9. Boozan, C. W., and Cohen, I. J.: Ophthaine: A new topical anesthetic for the eye: Am. J. Ophth., **36**:1619-1621 (Nov.) 1953.
10. McIntyre, A. R., Lee, L. W., Rasmussen, J. A., Kuppinger, J. C., and Sievers, R. F.: Laboratory and clinical trials of five local anesthetics. Nebraska State M. J., **35**:100 (Apr.) 1950.
11. Bellows, J. G.: Surface anesthesia in ophthalmology. Arch. Ophth., **12**:824-832, 1934.
12. Scheie, H. G.: Discussion of Schlegel and Swan. Arch. Ophth., **51**:669, 1954.
13. Wilmer, W. H., and Paton, R. T.: Pontocaine as a local anesthetic in ophthalmology. Am. J. Ophth., **16**:106-108, 1933.
14. Bochner, M. K.: Use of Nupercaine in ophthalmology. Arch. Ophth., **10**:763-767, 1933.

MANIFESTATION OF BACTERIAL ALLERGY IN THE EYE*

A STUDY OF 35 CASES REFERRED TO THE INTERNIST FOR A SEARCH FOR FOCI OF INFECTION

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INTRODUCTION

During the past decade, there have been a number of additions to our knowledge concerning the mechanism of allergic reactions. The present review is an integration of these newer concepts into the classification and management of allergic disorders of the eye. In this study, emphasis has been placed on the mechanism of bacterial allergy. A group of patients referred by the ophthalmologist to the internist for a search for foci of infections is the basis for this study of allergic mechanisms. Few conclusions have been reached at this time. The purpose of this presentation is to report on progress to date.

GENERAL RELATIONS BETWEEN OPHTHALMOLOGY AND IMMUNOLOGY

Bacterial allergy in medicine has been a controversial and little understood subject from the time that the tuberculin reaction was first described by Robert Koch in 1891.[1] Bacterial allergy in ophthalmology also has been a controversial subject.

The eye, however, is well adapted to the study of allergic processes for in it can be seen the role of vascularization, responses to whole bacteria and their soluble components, as well as the results of humoral influences, endocrines, drugs, and local tissue factors. The eye also is well adapted to the study of host responses to foreign substances, for example, reactions to temporary transplants such as cornea[2] and permanent transplants such as tumors.[3]

It is not surprising, therefore, that ophthalmologists have been respected contributors to our knowledge in this field. From them have come studies on the focal reaction in the eye to tuberculin given elsewhere to the host,[4] the role of autosensitization in sympathetic ophthalmia,[5,6] and the local effect of cortisone on inflammation.[7]

BASIC ALLERGIC MECHANISMS

A review of basic allergic mechanisms is helpful in understanding any classification of allergy in the eye. For the purpose of this survey, allergic reactions in the eye have been divided into two fundamental types—*immediate*, or anaphylactic allergy, and *delayed*, or bacterial type allergy (table 1).

Immediate type allergy can be graphically presented, as in Figure 1. It is seen that an antigen, which is either a protein or a simple chemical compound (hapten) linked to a protein so that it becomes a complete antigen, is the agent which sets the allergic response in motion.

This reaction is accomplished by the antigen first combining with certain cells of the host. These are sometimes called the shock organ. This combination does not itself injure the cells, but rather renders the cells sensitive to injury when an antibody to the specific antigen then combines with the antigen on the cell surface. Antibody also can combine with tissues harmlessly. Tissue injury then occurs when antigen reaches the site of combination.

Immediate-type allergy usually involves the walls of capillaries and certain smooth muscles of the host. The first result of this combination of antibody with sensitized cell is the release of histamine and histaminelike substances. This causes capillary dilatation, or the flair of a hive, and, as plasma leaks out of the blood vessel, the later wheal of the hive. The smooth muscles involved produce

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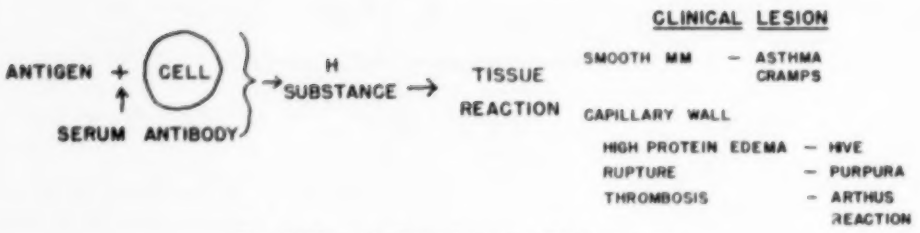

Fig. 1 (Favour). Immediate-type allergic reaction.

various responses; for example, the bronchospasm of asthma. More intense immediate-type reactions result in greater damage to the capillaries leading to hemorrhage into the tissues (purpura) and thrombosis (Arthus reaction).

This is a conveniently oversimplified, essentially accurate model of immediate-type allergy. It will perhaps not confuse this picture too much to indicate that some antigens and some haptens have much greater potency than others as allergens. Furthermore, some individuals possess inborn cellular traits which make them more susceptible than others to allergic manifestations.

The second major type of allergic reactions is the tuberculin-type, or *delayed-type* of allergic reaction. For convenience, the tuberculin-type reaction will be used as a working example of bacterial allergy. This is because there is a great deal more known about the mechanism of the tuberculin reaction than there is about delayed-type reactions associated with other infections. It is also used because the underlying principles which hold true for tuberculin allergy apply equally well to these other infections and to their ocular complications.

Unfortunately, bacterial allergy is not a precise term. Sometimes both immediate type

TABLE 1

CLASSIFICATION OF EYE DISEASE BY ALLERGIC TYPES

(Adapted from Woods)

Structure	Disease	Type of Reaction
Conjunctiva	Hayfever conjunctivitis	Immediate
	Vernal catarrh	Immediate and allergic diathesis
	Eczematous conjunctivitis	? Combination immediate & delayed
	Recurring irritational conjunctivitis	Predominantly delayed
Cornea	Superficial keratitis	
	Phlyctenules	Predominantly delayed
	Marginal ulcers	? Direct toxin effect Delayed allergy
	Deep keratitis	Mixed, immediate & delayed Direct invasion by agent
Uveal tract	Autosensitization	
	Endophthalmitis phaco-anaphylactica	Mixed, immediate & delayed
	Sympathetic ophthalmia	Delayed
	Nongranulomatous uveitis	Delayed
	Granulomatous uveitis	Mixed, immediate & delayed Direct invasion by agent

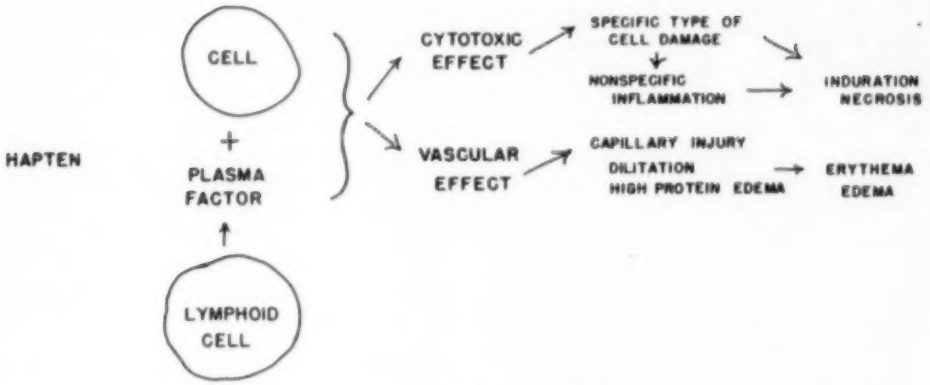

Fig. 2 (Favour). Delayed-type allergic reaction.

and delayed type tissue responses may complicate bacterial infections, depending upon the bacterial product which is liberated by the invading organisms. Hereafter we will use the term "delayed-type reaction" where it is usually applied to bacterial allergy.

In Figure 2 is given a model of the delayed-type reaction. It is seen that in this reaction, the antigen is not a complete antigen but is a compound of small molecular weight, usually a protein such as tuberculin or brucellergin. When it combines with cells of the sensitized host, these cells undergo direct destruction without the apparent intervention of any intermediary mechanisms. Cell destruction in turn leads to inflammation, the leaking of plasma and cells into the area, and, where intense destruction has taken place, to the necrosis of tissue with the eventual healing by scar tissue formation.

Microscopic studies on tissues[8] and time-lapse movies of the tuberculin reaction produced under lucite windows placed in rabbit ears[9] indicate that this process, like immediate-type allergy, begins promptly after tuberculin reaches the tissues. Gross evidence of tissue damage, however, takes longer to develop, hence the term "delayed-type" reaction.

Like immediate-type allergy, erythema is a characteristic but less marked feature of these responses. This can be seen directly in the ear-window studies as a generalized capillary dilatation. In the gross lesions, it is seen as a persistent erythema. Although edema accompanies delayed-type reactions, induration is the classic tell-tale progressive change which clearly distinguishes the tuberculin reaction from the hive.

It is more difficult to distinguish the Arthus type of reaction from the tuberculin reaction, since both the Arthus and tuberculin reactions may reach their peak after 24 hours, and both reactions may result in tissue necrosis. Although the morphologic separation of these reactions is a controversial subject among pathologists,[10] the two can be clearly differentiated by immunologic means.

There is always a high titer of circulating antibodies to the offending antigen when there is an Arthus reaction.[11] Similar antibodies are not present in the tuberculin reaction.[12, 13] Furthermore, the Arthus reaction can be passively transferred with high titer serum.[11] The tuberculin reaction cannot be so transferred.[14] We will return to the subject of the passive transfer of delayed-type allergy further on in the discussion of tissue sensitivity.

It has just been said that immediate type reactivity is characterized by a circulating antibody. In serum sickness which is one of

the well-studied forms of immediate-type allergy, this antibody can be measured by many test tube methods. There are precipitin tests, the complement-fixation techniques, and other laboratory tools.

Pollen allergy is a subdivision of immediate-type allergy. It differs from serum sickness allergy only in the nature of antibody, or reagin, which circulates in the plasma and which cannot be detected by the usual in vitro precipitin tests. Antibodies to pollens are measured in the living host by the passive transfer method. This is done either by injecting large amounts of antisera in a normal animal, or by intradermal injections of small amounts of serum which are allowed to fix to the tissues locally before injection of the antigen into the same site after 12 hours (Prausnitz-Kuestner reaction).

We have said that the delayed-type allergy ordinarily cannot be passively transferred with the serum as can be immediate-type allergy. It has been found recently, however, that tuberculin allergy can be transferred passively to a nonsensitive host by the use of certain cells from the tuberculous host. Cells derived from a tuberculous focus,[15] from lymph node pulp or peritoneal exudates,[16] and from the blood[17] of tuberculin-sensitive hosts will confer temporary tuberculin allergy on a normal host. Delayed-type allergy to streptococcus infections also can be passively transferred with the leukocytes of the peripheral blood.[18]

In other words, immediate-type allergy depends on circulating antibodies. Delayed-type allergy depends on certain cells of the sensitized host. Immediate-type allergy is predominantly a disorder of the vascular walls. Edema, with little cellular infiltration, and smooth muscle involvement, are other effects. Delayed-type allergy is predominantly an injury to tissue cells with secondary injury to capillaries.

The lesions of immediate-type allergy are more acute and more evanescent. The lesions of delayed-type reactions develop slowly and tend to become complicated inflammatory processes.

In both types of reactions, when they are severe, the initial response may act like a trigger mechanism in flooding the area with cells of the type which accompany inflammation. In delayed-type allergy, cells which passively transfer allergy may also join the reaction. These in turn may further augment tissue injury to a degree which is out of all proportion to the amount of the agent which initiated the process.

Recent developments in allergy

A series of recent observations on the tuberculin reaction sheds some light on the manner by which sterile focal eye reactions can accompany active infections in remote parts of the body. It is indicated in Figure 2 that tuberculin is a direct toxin for the cells of the sensitized host. This phenomenon was first studied on the cellular level in tissue cultures.[19] From these studies came the concept that all the cells of the sensitized host are sensitive to tuberculin.[20]

It has been pointed out that tissue culture studies, purporting to show that all the cells of the host are sensitive to tuberculin, have been done with the only cell types which will passively transfer tuberculin allergy.[21] Tissue cultures from sensitive animals done with cells of epithelial origin, such as dermis[22] and renal epithelium,[23] are not sensitive, even to very large amounts of tuberculin. Even exudate cells,[24] if they are all polymorphonuclear cells, are not sensitive to tuberculin, nor will they passively transfer tuberculin allergy from the sensitive to the nonsensitive host.[25]

It is quite likely that the majority of the body structures in the "tuberculin-sensitive" host are basically insensitive to tuberculin. Local tissue injury in "sensitive subjects," which does take place, occurs only when certain types of cells of the mononuclear series "passively transfer" tuberculin allergy from the region of a focus of infection from

which we know that they came,[14] to the remote site of injury. Since these special cells of the leukocyte series are known to circulate in the peripheral blood,[17] any process which induces inflammation, for whatever reason, may bring about their local concentration where there is inflammation. Under these circumstances, it is not surprising that remote manifestation of infections can occur once there has been a nonspecific local process to initiate a metastatic reaction.

A corollary of this concept is also true. Local tuberculin type reactivity must be a process which is constantly being renewed. It is not a static condition of the tissues. We know that tuberculin allergy soon disappears unless viable organisms are present somewhere in the body to keep it up.[26] We know that tuberculin allergy transferred by means of cells lasts only a few days.[16] We also know that tuberculin allergy is quite variable from week to week in sensitive persons.[27] It is altogether likely that delayed-type reactions in the eye are not exceptions to this principle.

Another interesting approach to this problem has been offered by Favour and his group. These workers have tagged tuberculin with I^{131}.[29] This can be done without altering its biologic potency. When tagged tuberculin is added to heparinized whole blood, it is firmly absorbed on the leukocyte in quantities greater than can be accounted for by simple ingestion. Similar studies in which tagged tuberculin is given intravenously[29] to the intact normal animal indicate the same process is operative. This adsorption is unrelated to tuberculin allergy in the host. Red cells do not take up tuberculin under the conditions of these experiments.

Other evidence that white blood cells adsorb tuberculin has been offered by Boyden, who has shown that leukocytes which have taken up tuberculin can be agglutinated by a specific antisera.[30]

In this type of study we have a second mechanism by which the blood stream may furnish the ingredients of a delayed-type reaction to areas where some minor inflammatory process has brought out a leukocyte response. For many reasons, tuberculin probably does not circulate as a free substance in the plasma of the tuberculin-sensitive host.[31] We do know that tuberculin can be carried by leukocytes.

In this connection it should be pointed out that studies with isotope-tagged Shiga toxin reported by Braude[32] also have shown that peripheral blood leukocytes take up significant amounts of other soluble bacterial products.

It now remains to be shown that leukocytes can transport to, and localize in, the uveal tract, both tuberculin-type bacterial products as well as tissue-sensitizing factors carried by cells derived from remote infectious processes. Indirect evidence that this does occur is impressive.

If this can be shown directly, many mysteries about uveal allergy will be cleared up. For one thing, there need not be septicemia for products of an infection to reach the eye through the blood stream. For another, it is apparent that a single variable cannot be expected to account for the variegated pattern of allergic eye manifestations. Like so many other biologic phenomena, there is no single all-or-none cause of an allergic eye reaction.

Close study of individual patients has long impressed clinicians that exacerbation in areas of infection capable of feeding various byproducts of a purulent response into the blood stream often have coincided with recurrent attacks of uveitis. The lack of regularity of this relationship has dampened enthusiasm for accepting the focus of infection mechanism warmly as a cause of uveitis. This type of epidemiologic information as a means of finding a cause of a given disease is most helpful in the analysis of a single factor disease mechanism. It is

much less adequate for the analysis of the multivariable systems operative in allergy of the eye. Additional laboratory methods for measuring the presence or absence of allergens, and the specific and nonspecific host responses to them, are much needed.

Classification of allergic eye disorders

The classification of allergic disorders of the eye given in Table I indicates that many types of allergic syndromes are not pure forms but are combinations of immediate and of delayed-type reactions. In these circumstances the causative agent may be liberating multiple factors. Some of these are highly antigenic complete antigens such as the bacterial toxins or bacterial polysaccharides and others are highly active haptens like tuberculin or brucellergin. In still other circumstances, two separate sources of antigens may be present—for example hay fever and chronic infection.

There are two features of this classification which are purposely left out of the preceding discussion on basic mechanisms. The first is the place of bacterial toxins in eye disease. The second is the nature of granulomatous reactions in eye disease. These initial omissions were done in the interest of clarity.

Bacterial toxins in eye disease

Bacterial toxins are among the most potent cell poisons known. These toxins produce their effects by diverse means. Diphtheria toxin interferes with the cytochrome system of cell respiration.[33] The alpha toxin of Cl. Welchii is a lecithinase.[34] Other toxins are neurotoxins.[35] None of these toxins is an important cause of eye pathology. Unfortunately, other bacterial toxins, more likely to take part in eye disease, have not been so well characterized, nor are there immunologically pure preparations available for their study. Except for so-called staphylococcus "toxin,"[36] bacterial toxins are not known to be a major factor in eye infections.

The evidence for staphylococcus toxin as a cause of eye disease is tenuous. Highly purified toxin comparable to preparations of diphtheria toxin have not been used to produce the clinical syndromes which are supposed to be related to staphylococcus toxin producing infections of the eye. Furthermore, the immunity induced by toxoid is antitoxic, not antibacterial.[37] Even the successful use of staphylococcus "toxoid" for the immunization of a patient with staphylococcus blepharitis, for example, is not clear evidence that the disorder is due to toxin liberated, nor is a cure necessarily the result of antitoxin elaborated by the host. The crude materials used for these toxoids contain many other bacterial proteins including those which will elicit agglutinins and precipitins, as well as those which will cause typical delayed-type reactions. Immunization with "toxoid," as commonly practiced, is a mixed type of stimulus. In the series of patients reported with this study, we have had successful therapeutic results in chronic staphylococcus infections using heat-killed, washed whole bacterial vaccines which have been freed of their exotoxins.

Granulomatous eye disease

Granulomatous reactions are also poorly understood pathologic entities. They are one of the most primitive cellular responses of the animal body to invading parasites. Insects which do not possess the elaborate systems for antibody formation found in higher animals[38] are capable of forming granulomatous reactions around agents which cannot be destroyed through simple phagocytosis by the circulating leukocytes.[39]

It is thought that granulomatous lesions in human eye disease also contain concentrations of the causative agent or parasite which cannot be readily destroyed by the host.[40] In this respect they differ from the lesions of immediate and delayed types of allergy which are brought about by the soluble and not the particulate components

of an irritative process, and resemble reactions induced by particulate antigens.[41]

For example, tuberculous granulomas contain tubercle bacilli either alive and multiplying, or inactive and dead, but in such concentration and physical state in caseous tissue that they form a poorly soluble focus. If there is no appreciable allergic response to this focus, as with certain parasites,[42,43] the problem is one of primary structural impairment. If allergy complicates the focus, it may greatly overshadow the actual extent of the lesions by a marked enveloping reaction.

There are certain features about the immunologic isolation of the inner structures of the eye which are much like the situation in the central nervous system of higher animals and in the inner milieu of insect tissues. The eye will tolerate a foreign tissue, as in the transplantation studies already mentioned, for an indefinite period, so long as an inflammatory response is not aroused. The same tissue transplanted elsewhere in the host is promptly rejected after one to two weeks by complex reactions which are probably allergic in nature.[44]

These observations suggest that living parasites within the eye are not easily reached by normal immune or allergic host responses. Accordingly, their elimination by the host is a difficult matter.[45,46] On the other hand, an inflammatory response which permits the exudation of cells and plasma into the structures of the eye changes its immune and allergic status to that approximating the rest of the host but, in so doing, may lead to destructive results due to the intense response to previously protected reservoirs of antigenic substances accumulated in the eye structures during quiescent phases of earlier tissue invasion.

This brief schematic presentation of the basic allergic types has the merit of permitting an equally oversimplified classification of allergic reactions involving the eye, summarized in Table 1.

Lesions of the eye which are characterized by erythema, and edema of rapid onset, very likely are predominantly immediate-type reactions. Their cause, therefore, may be sought in the category of agents which will elicit this type response. On the other hand, lesions of the eye which are characterized by slower development, by induration, by a tendency to become necrotic, to ulcerate, and to heal by the formation of scar tissue —these lesions are predominantly delayed-type allergic reactions. Their cause should be sought in a source of a hapten, usually from a part of the body remote from the eye, usually an infectious process, and usually caused by an organism which is capable of surviving within the host by virtue of walled-off loci impervious to an otherwise effective immunity or even to the proper use of antibiotics.

Finally, lesions of the eye which are characterized by localized inflammatory processes leading to early structural alterations in tissue and dramatic fluctuation in responses, of the type seen in both immediate and delayed-type reactions—these lesions are examples of granulomatous uveitis. Their cause should be sought in an invading parasite lodged within the eye lesion itself as well as harbored elsewhere in the host.

The management of these three types of eye disease will be discussed briefly in the consideration of the clinical material which follows.

Medical evaluation of patients with blepharitis and uveitis

Procedure for patient evaluation

Patients in this series were selected by referring physicians because of a recurrent course which had been present for some time. In most instances, a previous medical evaluation had been made. Usually one or more courses of an antibiotic had been given. Before the cortisone era, symptomatic medication had been used. Since the cortisone era, patients with anterior uveal tract disease were maintained on cortisone locally

TABLE 2

THIRTY-SIX SELECTED PATIENTS WITH RECURRING EYE DISEASE

Etiology	No. Patients	Treatment	Results	Follow-up
Iritis				
Highly likely				
Tuberculosis	1	Old tuberculin	Remission	4 yr.
Chronic prostatitis				
Staphylococcus	1	Autogenous vaccine	Remission	3 yr.
	1	Autogenous vaccine	Remission Retreatment 2 yr. later	2 yr.
Likely				
B. hemolytic streptococcus	1	Penicillin	Remission	3 yr.
	2	Penicillin	Occasional attack when off PCN	2 yr.
Infected colostomy	1	Surgery	Remission	4 yr.
Coincidental dental sepsis	5	Hygiene & antibiotics	Recurrences within 6 mo.	2 yr.
	1	Hygiene & antibiotics	Remission	4 mo.
Cause uncertain	2	Hygienic measures Antibiotics Immunizations	No change	4 yr.
	4	Immunizations	Milder & fewer attacks	2 yr.
	1	Hygiene & antibiotics	Milder & fewer attacks	1 yr.
	1	Hygiene & antibiotics	Remission	6 mo.
	21			
Other types of uveitis				
Recurrent vitreous hemorrhage (Eales'disease)				
Tuberculosis	1	Old tuberculin	Remission	4 yr.
Dental sepsis	1	Streptomycin plus PAS	Recurrence	1½ yr.
Retinitis				
Brucellosis, possible	1	OT and brucellin	Remission	2 yr.
Brucellosis, probable	1	Brucellin	1 recurrence	1½ yr.
Toxoplasmosis, likely	1	Daraprin	Recurrences	1 yr.
Not definite	1	OT plus A autogenous vaccine	Recurrences	2 yr.
Chronic scleritis				
Staphylococcus	1	Autogenous vaccine	Remission	2 yr.
Dental sepsis	1	Hygiene & extractions	Remission	4 yr.
Terrians dystrophy				
Ulcerative colitis, likely	1	Antibiotics	Recurrences	1 yr.
Chronic conjunctivitis				
Staphylococcus	1	Autogenous vaccine	Improved	1 yr.
	2	Autogenous vaccine	Recurrences	3 yr.
Recurring corneal ulcers				
Staphylococcus	2	Autogenous vaccine	Remissions	1 yr.
	1	Autogenous vaccine	Recurrences	6 mo.

during periods of acute symptoms.

In Table 2 is given summary information on 36 patients who were studied by the internist for an infectious cause of their eye difficulty. In history taking, attention was focused first on the chronologic listing of the eye symptoms. Dates were obtained to the nearest month. Most patients were able to give an excellent account of their eye symptoms since the interruptions in their

daily life by their illness were quite dramatic. Dates were written down as obtained in order to get an unbiased time sequence which could later be correlated with other medical events, such as dental extractions, or the use of antibodies. A history of family or personal allergy was sought.

In the system review, the record was sought for acne, boils, dermatitis, recurrent sinus trouble of a serious nature, tonsillitis, and cervical adenitis. A chronologic dental history with specific dates was then taken. During this questioning, no mention of eye symptoms was made until it was complete. When this was then compared to the time sequences of eye symptoms, it was surprising both to the patient and to the doctor how often this device turned up an obvious correlation between an attack of eye trouble and a major dental procedure.

The most difficult types of infection to evaluate were dental periapical disease and gingivitis. Both of these conditions can shed bacteria and their products into the blood stream during simple chewing. It is also known that these diseases uniformly lead to transient septicemia during dental procedures,[47] even while the patient received an effective antibiotic.[48] Denervated teeth are particularly hard to evaluate. Apparently healthy teeth also are hard to assess. A patient will have mild subjective discomfort in a tooth which is "sound" by X-ray examination and by a pulp test. The dentist accordingly assures the patient that all is well and is surprised when the patient returns within a few days with an acute apical infection requiring extraction. X-ray films, after all, do not detect bacterial infections until long after gross structural changes are present.

In men, particular attention was paid to a history of prostatitis and of past treatment by massage. Here again, surprising correlation between prostatitis and eye symptoms or of massage treatment and eye disease occasionally turned up when dates were recorded and then later compared with other parts of the recorded history.

The well-known occurrence of iritis in patients with rheumatoid arthritis[49] was kept in mind.

Epidemiologic results

History of allergy (hives, hayfever, asthma, rashes)—8/32 or 20 percent.
History of acute dental infection coincident with eye disease—8/36.
No teeth—2/36.
Chronic bronchial infections—2/36.
Chronic empyema—1/36.
History of tuberculosis—0/36.
History of tuberculosis contact—2/36.
History of gastrointestinal infection—2/36.
History of rheumatoid arthritis—2/33.
History of arthritis nonspecific—10/33.
History of rheumatic fever—1/33.
No obvious clue by history—10/36.

In the physical examination, special attention was paid to the skin, paranasal sinuses, gingiva, teeth, tonsils, bronchii, and prostate. Chronic infection in these areas was often found (table 2). No instances of significant chronic cervicitis was encountered. Other infected areas were found —for example, chronic empyema, ulcerative colitis, and an infected colostomy stoma. No doubt this list could be extended if the series were larger.

Extensive laboratory procedures were carried out on individuals hospitalized. Most of the patients were studied one or more times in a hospital. Routine laboratory tests included a chest film, full mouth survey dental films, blood and urine studies, cultures, and skin tests. Skin tests were found to augment cultural information regarding infections and in many instances to be a more accurate guide as to extent and duration of infection than any other simple means available to us.

Skin testing procedures

Cutaneous skin tests were done with several testing agents (table 3). Bacterial

TABLE 3

BACTERIAL SKIN TESTS, TYPE OF EYE DISEASE, AND COINCIDENT INFECTION IN 36 PATIENTS

Number	Patient	Dx	Significant Infection	Allergy	Arthritis	PPD	Strep.	β Strep.	D. pneumonia	Staph. aureus	Brucella	Other Features
1	F. H.	Iritis, recurrent	β Strep.	0	+	1°2 +	2 +	4 +	0	2H	?	
2	O. F.	Iritis, recurrent	β Strep.	0	+	2°1 +	1 +	4 +	0	±	±	
3	M. H.	Iritis, recurrent	? β Strep. ? Teeth	0	+	1°2 +	±	4 +	0	+	0	
4	K. H.	Iritis, chronic		0	0	2°1 +	0	4 +	0	2 +	0	School teacher. Recurrent environmental exposure. β strep.
5	B. T.	Iritis, chronic chorioretinitis		0	0	1° ±	4 +	4 +	1 +	±	?	
6	C. H.	Iritis, chronic	? Teeth	0	0	1°2 +	±	2 +	0	1 +	?	
7	R. L.	Iritis, chronic		0	+	1°2 +	±	+	0	1 +	0	
8	H. P.	Iritis, recurrent		0	+	1°3 +	±	±	0	0	?	
9	A. R.	Iritis, recurrent	Teeth ? bronchitis	0	+	1°2 +	0	+	0	0	+	
10	W. W.	Iritis, recurrent		0	0	1° ±	2 +	±	0	0	0	
11	G. F.	Iritis, recurrent	? Teeth ? Tonsils			0	0	1 +		0	0	
12	A. R.	Iritis, recurrent	? Tonsils	+	0	0	0	0	±	0	0	
13	P. S.	Iritis	Teeth	0	+	2° ±	0	+	0	0	0	History RF. Rheumatic heart disease.
14	L. B.	Iritis, recurrent	? Teeth	0	+	2° ±	+	+ + +	±	0	?	Rheumatoid arthritis
15	G. B.	Iritis, recurrent										
16	F. B.	Iritis, chronic	Prostate	0	0	2°1 +	0	+		+	0	Sarcina 1 +
17	P. B.	Iritis, recurrent	Prostate	+	0	2°2 +	±	±	±	+	2 +	M. Tetragenous 1 +
18	S.	Iritis, recurrent	Colostomy	0	0	2°1 +	3 +	±	0	±		E. Coli 2 +: Enterococci 2 +
19	R. B.	Iritis, recurrent	? Teeth	0	+	2° ±	+	±	0	0	±	Rheumatoid arthritis
20	W. H.	Iritis, recurrent	? Teeth	+	0	0	+	+	2 +	±	1 +	
21	A. R.	Choroiditis, recurrent	Tonsils & prostate	0	0	2°1 +	±	±	0	2 +	?	Sarcina ±
22	R. L.	Retinitis, recurrent	? Brucella ? TB	0	+	2°4 +	±	2 +	±	3 +	±	
23	F. K.	Retinitis with recurrent hemorrhages	Probable TB	0	0	1°1 +	0	±	?	0	?	
24	D.	Retinitis, recurrent	Probable toxoplasmosis	+	0	2°2 +	±	±	?	0	0	
25	D. B.	Terrians dystrophy	Ulcerative colitis	0	0	0	0	1 +	0	0	0	
26	I. R.	Retinitis, recurrent	? Brucellosis	0	0	1° ±	0	2 +	0	0	4 +	
27	G. B.	Corneal ulcers recurrent	Staph.	0	0		±	±	0	±		
28	B. L.	Scleritis, chronic	Staph.	+	0	0	0	0	1 +			
29	W. M.	Conjunctivitis, chronic	Staph. empyema	0	0							
30	H. M.	Corneal ulcers, recurrent	Staph.	0	0	0	0	0	0	0	0	
31	R. H.	Corneal ulcer, recurrent	Staph.	0	0		0	0	0	0		
32	F. K.	Conjunctivitis, chronic	Staph.	0	0					2 +		
33	H. C.	Vernal conjunctivitis infection	Secondary staph. infection	+	0	2°1 +	0	0	±			
34	C. T.	Scleritis, chronic secondary iritis	Teeth	+	+	2°1 +	2 +	1 +	0	0	0	Associated erythema nodosum
35	S. ?.	Retinitis with recurrent hemorrhage		0	+	2°1 +	2 +	1 +	±	0		
36	A. K.	Iritis, chronic	Prostatitis	+	0							

vaccines were prepared from heat-killed, washed, saline suspensions of organisms. These preparations were used as a 1:10 dilution of a standard vaccine containing approximately 9×10^8 organisms per ml. for skin testing and as undiluted vaccine for treatments. The 1:10 dilution was found to produce no reaction greater than 10 by 10 mm. induration at 24 hours and no induration at all at 48 hours in healthy control subjects. Control subjects with clinical infections due to these organisms showed delayed reactions greater than 10 by 10 mm. induration at both 24 and 48 hours.

The same range of cutaneous sensitivity to bacterial vaccines was seen as that noted in tests with tuberculin, with brucellergin, and with other commercial testing materials. The few individuals with marked delayed-type reactions to staphylococcus vaccine

showed areas of central necrosis maximal at 48 to 72 hours. In general, the positive delayed-type reactions to the bacterial vaccines were essentially the same in appearance, sequence, and range of intensity as were the positive tuberculin reactions.

In some patients we observed a curious recrudescence of intracutaneous skin tests which had been placed as long as a month before. These return reactions recapitulated the original positive reaction but with less intensity. Some occurred within 48 hours after receiving subcutaneous doses of the homologous bacterial vaccine. Usually the old skin test site, which reacted, was homologous to the vaccine administered. This was not always so. Sometimes four different skin tests which had been placed on the same day would all light up again as part of this reaction. At other times, these rebound reactions occurred in untreated patients during the first few days of a simple nonbacterial upper respiratory infection which was documented as such by cultures of the nose and throat. Sometimes the skin recrudescence coincided with a reactivation of eye symptoms. At still other times, return reactions occurred for no apparent cause. They were usually seen in persons who had had strongly positive reactions when first tested.

The degree of bacterial allergy to streptococcus antigens and to tuberculin is known to fluctuate in sensitive subjects.[27] This variable behavior of a known deposit of nonviable bacterial products in a tissue site is a reflection of the delicate balance of forces in the sensitive subject which are competing either to augment or suppress delayed-type tissue reactions.

If in one's imagination the word "eye" is substituted for "skin" (and the eye and skin do have common embryologic origins), these experiments of nature observed in patients are more informative than at first is apparent. They suggest that bacterial products do get into the eye, where they may lie dormant for a reasonable time, doing no harm. They may then cause a reaction at a time when the whole host becomes more sensitive. This can occur during the recurrence of the same type of infection elsewhere in the host.

It also may be coincident with an exacerbation of a different infection, much like an anamnestic reaction which acts to alter sensitivity nonspecifically; or it may be the result of other homeostatis mechanisms, such as fluctuations in adrenal activity, which are not themselves symptomatic. These local reactions, however complex, nevertheless are dependent first upon a specific tissue sensitivity of a significant degree.

There was often a considerable overlapping in the degree of reaction sizes of several antigens in persons sensitive to the beta hemolytic streptococcus. In these individuals, reactions to alpha hemolytic streptococci and to D. pneumonia testing material were usually also positive. Where an alpha streptococcus was the likely chronic infection, as in a respiratory or in a dental infection, the alpha streptococcus skin test was large, but little different from the beta streptococcus skin test, and rarely as strongly positive as the maximum reactions to tuberculin, brucellergin, and beta streptococcus vaccine which were seen in the group as a whole. Common antigens in the alpha and beta streptococcus and pneumococcus probably account for these cross-reactions.

Reactions were read at 24 and 48 hours. The area of erythema and induration was noted. Most skin tests showed some induration up to 5 by 5 mm. at 24 hours, which was gone at 48 hours. This was called a negative reaction. Induration of 5 by 5 to 10 by 10 mm. was graded as ±. Positive reactions were considered significant if they were greater than 10 by 10 mm. or induration at 48 hours. Reactions with induration at 48 hours of 10 to 20 mm. in diameter were graded 2+, greater than 20 mm., 3+, and those with central necrosis, 4+. These criteria are the same as those used widely for interpreting the tuberculin test.

Normal subjects harbor enough symbiotic staphylococcus and streptococcus infections in their tissue at all times to show some degree of reactivity to these testing agents. The only exceptions encountered were individuals who had just completed a protracted course of intramuscular penicillin injections. This anergy may last for several months. Systemic cortisone treatment and the use of ACTH will also produce a similar suppression of skin reactivity. This steroid suppression of hypersensitivity lasts only as long as treatment is continued.[27]

It was our impression that the most certain evidence that antibiotic or other specific treatment had eradicated an infection from a patient's system was the loss of all delayed-type sensitivity to the causative organism. This was used as a therapeutic goal in the management of these eye patients. This goal often could not be reached. The persistence of marked delayed-type allergy in a patient was interpreted as an ominous sign that little was being done to alter the natural course of his disease.

The bacterial vaccines used for these skin tests were crude preparations containing many components of the original organisms. As might be expected, immediate-type reactions were encountered occasionally. These occurred more frequently with staphylococcus vaccine. Sometimes they correlated with the presence of a recent respiratory tract infection. These reactions were not limited to the use of crude materials for we have seen the same phenomenon on several occasions when PPD has been used. In these reactions, the wheal and flair began within 30 minutes, and reached as great a size as 3 by 3 cm. at two hours. Edema and redness cleared progressively by six to eight hours. Thereafter, a delayed-type reaction was observed. In some subjects, the subsequent delayed reaction was not significantly enlarged at 48 hours. In others, a typical positive test was present at 48 hours.

Bacteriology

Appropriate cultures were obtained from the conjunctival sac, nose, pharynx, extracted teeth, removed tonsils, skin, prostate, and various sinuses of the patients of this study. The data form an excellent compendium of the organisms which can grow in these areas. As expected, the staphylococcus aureus, frequently hemolytic and coagulase positive, was recovered from the conjunctiva in patients with conjunctivitis and recurrent corneal ulcers. The same organism also was regularly recovered from the nose of these patients. Following successful immunization, the staphylococcus usually persisted in both areas. Sometimes it did not. The same findings can occur in normal people.

Multiple throat cultures were made on all patients with uveitis. The pharynx occasionally harbored a pathogen such as the pneumococcus, influenza bacillus, or the beta hemolytic streptococcus. In three persons, the recurrent presence of a beta hemolytic streptococcus in cultures of the pharynx led us to believe that this organism could be the cause of eye symptoms. The negative findings in other patients and certain coincidental relations between pharyngitis and iritis in these patients strengthened these suspicions (table 2). Persistent significant delayed-type skin reactivity in these subjects, despite penicillin treatment, was also present. It is likely that these examples of iritis are due to "deep" streptococcal infections. They are not proven relationships.

Patients suspected of having tuberculosis were subjected to gastric lavage for cultures for tubercle bacilli. Many others of the patients hospitalized were similarly cultured. No cultures were positive for tuberculosis. The one likely example of tuberculosis in this series is a reflection of the infrequency of clinical tuberculosis in the population of this area. A similar low incidence of tuberculosis as a cause of erythema nodosum in this geographic area has also been reported.[30] This clinical syndrome is cited since it too is an example of local pathology resulting from a remote infection which, by itself, may be trivial. The one patient in this series who

had both uveitis and erythema nodosum is a token of this rationalization.

Discussion of epidemiologic, physical, and laboratory findings

In 32 patients on whom allergic information was complete, there were eight with some type of past allergic reaction, and one additional patient with a family history of allergy. These included attacks of hives, seasonal hayfever, asthma, and cutaneous eruptions. This is the expected incidence (20 percent) of allergy in an unselected population.[51]

There were eight of the 36 patients in whom one or more attacks of eye disease were associated with acute dental infections. In this series of patients, there were two who certainly did not have dental infection as the cause of their eye disease. They had no teeth.

One of these patients had a chronic prostatitis which long antedated his iritis. His chronic eye disease showed acute relapses on several occasions when his prostatitis was active. During these times it was worse the morning after intercourse. And on two occasions a mild flare-up occurred during hospitalization the day after prostatic massage for cultures. It also flared up on one of the occasions when the patient was skin-tested with autogenous vaccine made from a sarcina recovered from prostatic secretions. This skin-test reaction was positive. The patient's prostate and eye disease subsided coincident with autogenous vaccine treatment. This story is convincing circumstantial evidence of a causal relation between iritis and prostatitis. As good evidence as this is unusual.

The second patient had had five attacks of iritis before being admitted to this study. Two of these occurred after dental procedures. His remaining few teeth which were in poor condition were removed. He was then edentulous, well, and happy for one year—a longer interval than that between previous episodes of iritis. Thereupon he had a mild recurrent attack of iritis associated with a seasonal respiratory infection. It was postulated that alpha streptococci could have been the offending organism during both episodes, first in the teeth and second in the pharynx, where they are present in all people. The patient then developed still another mild recurrence, this time unassociated with any evidence of infection. He was one of the patients who periodicaaly harbored a beta hemolytic streptococcus in his throat and showed a persistently strongly positive beta hemolytic streptococcus skin test, despite repeated penicillin treatment. The only reasonable explanation which could be found for the last attack was that the patient was "run down and tired." His work and sleep record did show evidence for this, but being "run down" cannot be measured.

These two stories are clear evidence for one conclusion. Patients with no teeth can have iritis.

The role of the teeth in eye disease in the other 34 patients is uncertain. The dentulous patients in the iritis group and most of those in the other groups, like most Americans, were shamefully and steadily losing their teeth. Although there is much controversy over the causes of this American tragedy, there can be little doubt that neglect of oral hygiene and diet which ends each meal with something sweet, are major factors. In many of these patients, efforts to get a good diet history were thwarted, much as efforts to get an alcoholic history are glossed over by the pathologic drinker.

Chronic bronchial infection was presented in two individuals. It bore no apparent relation to eye symptoms. One patient with a chronic draining empyema from which staphylococcus aureus repeatedly was recovered, suffered from a chronic staphylococcus blepharitis. On some, but not on all, of the occasions when he developed a lower respiratory infection, both his sinus tract and his eyes flared up.

Tuberculosis was not a likely cause of trouble in this small series of patients. No past history of tuberculosis was obtained. A

history of family contact was obtained twice.

In one of these persons with recurrent vitreous hemorrhages (Eales' disease), the tuberculin reaction was the strongest of the reactions tested. This patient became asymptomatic after tuberculin treatment.

In the other patient, multiple delayed-type sensitivities were present. This patient became asymptomatic after combined brucellin and tuberculin treatment.

Tuberculin treatment was given without success to three other patients with negative past and family histories and weakly positive tuberculin reactions. This was done as one of a series of vain efforts to stop the progress of their eye disease, more because of the tradition that tuberculosis is the cause of uveitis than because of any factual evidence for this etiology.

Attention was drawn to the gastrointestinal tract as a source of infection in two patients. One had iritis. This flared up twice (out of three attacks) coincident with obstruction, infection, and bleeding in a colostomy. Earlier penicillin therapy in this patient had been followed by the establishment of E. coli in this patient's nasopharynx as the resident flora. The iritis did not recur after oxytetracycline therapy and surgical revision of the stoma. E. coli disappeared from the nasopharynx coincident with this therapy. The other patient with gastrointestinal disease had smoldering active ulcerative colitis. Progressively active Terrians dystrophy appeared several months after the onset of colitis and on several occasions flared up above its base line of activity coincident with some, but not each, exacerbation of colitis.

In the 33 patients quizzed specifically about joint symptoms, two had frank rheumatoid arthritis and one a history of migratory polyarthritis and rheumatic heart disease. Ten other patients gave a history of incapacitating arthritis lasting longer than a month, one or more times in the past. Most of these attacks were unrelated to eye symptoms. This is a surprising incidence of joint disease in patients with eye disease. It is known that there are approximately 20 persons who develop some form of atypical arthritis for each person who develops classic rheumatoid arthritis. In these 10 patients, their disease was nondeforming, transient, and otherwise nonspecific. One of these was a clear-cut example of rheumatic fever followed by aortic insufficiency. Iritis did not coincide with the rheumatic fever.

There were 10 of the 36 patients who gave no obvious clue of a cause of their eye disease from physical examination.

Management of ocular infections

In this group of patients the acute symptoms of anterior uveal tract disease were kept under control by the use of various mydriatics and the local instillation of cortisone drops. Posterior uveal tract disease was handled expectantly until a reasonable diagnosis was made. The discussion here has to do with other forms of medical management which are aimed at the prevention of recurrent or chronic disease.

Two clinical principles were followed. When possible, the suspected allergen or invading agent was removed from the host. This first principle is an ideal goal which is rarely accomplished. When the probable source of trouble could not be removed, the second principle of "block its action" was pursued. When neither approach was helpful, the original nonspecific management was continued.

The first principle of "remove the allergen" can hardly be challenged when it has to do with airborne antigens. Sometimes ingenuity is required to ferret out the cause. A careful history, the use of skin tests, a change in the patient's habits—any one of these methods may give the cause and lead to effective therapeutic results in handling airborne or contact types of ocular allergy. This is not the point of emphasis of the present discussion.

Removing causative bacteria is just as sound treatment for bacterial allergy, but

it is much more difficult to do. Sometimes this can be done with antibiotics. It is unusual, however, to have ocular bacterial allergy which can be controlled by antibiotics alone.

This approach was successful in one of three patients treated with long courses of parenteral penicillin who had recurrent B. hemolytic streptococcus infections as the probable cause of iritis. In the other two, an oral prophylactic penicillin program prevented attacks while it was continued. These latter two patients often tired of taking medicine at every suspicion of a respiratory infection. Mild iritis recurred, twice in one and once in the other, while off medication (table 2).

The majority of conjunctival and corneal problems, and some examples of iritis, were associated with infections by organisms of the micrococcus family. These bacteria could be suppressed during acute infections with antibiotics as long as drug resistance did not develop. In time, infections became drug fast and chronic.

One patient with chronic conjunctivitis and one with chronic recurring superficial corneal ulcers were cured with autogenous staphylococcus vaccine therapy. The same treatment suppressed recurrence of disease in one patient each with corneal ulcers and with conjunctivitis. Treatment was continued to maintain improvement.

One patient with staphylococcus blepharitis failed to benefit at all from staphylococcus vaccine.

One patient with recurring iritis probably secondary to chronic prostatitis and nasopharyngitis, from both of which body regions a hemolytic staphylococcus aureus was recovered, received staphylococcus vaccine for a protracted period. One minor recurrence took place in an observation time of three years. Previous attacks occurred two to four times a year.

One patient, previously mentioned with iritis secondary to prostatitis, went into remission following a course of autogenous vaccine made from a sarcina recovered at a prostatic massage. Treatment was discontinued when eye symptoms subsided. Two years later, prostatitis and iritis recurred. Autogenous vaccine made from a hemolytic staphylococcus aureus recovered from the urinary tract again was followed by a two-year remission. Iritis was chronically active during the 10 years preceding vaccine therapy.

Most uveitis is a more difficult therapeutic problem. Twenty patients in this series followed for a period longer than the usual interval between their previous attacks (nine months to five years) reflect the many issues which arise (table 2). All but two patients in the uncertain etiology group had had recurrent disease of greater than one year's duration. Most of the patients have been followed for 20 months or longer, and some for five years.

Two of the 20 patients in the series were edentulous and therefore could not have had dental infections as the cause of their uveitis. One of these mentioned above had M. tetragenous prostatitis with a clear relation between prostatic and eye symptoms. The other also mentioned earlier was a recurrent carrier of beta hemolytic streptococcus in his pharynx and had a fair relation between iritis and pharyngitis. He also was the patient already mentioned whose teeth were removed.

Among the many other subjects, including those with tuberculosis or brucellosis as likely causes, dental infections were chronic. Six of 21 iritis patients and two of eight other forms of uveitis had frank dental sepsis. Each of the first six gave a history of dental procedures coincident with one or more attacks of uveitis. One of these ceased to have attacks of iritis following removal of remaining infected teeth. All of these individuals had other attacks of uveitis without frank dental sepsis. They were all dental cripples with a steady rate of decay in progress at all times. Since this is common in Americans of the same age group and of the

same improper dietary habits, it is a factor difficult to evaluate.

The usual bacteria causing dental infections is a member of the α or γ streptococcus family. Sometimes it is a staphylococcus, and occasionally it is an enterococci, or even a beta hemolytic streptococcus. Removing infected teeth or tonsils does not remove all the oral tissue infected with one or more of these organisms. Even removing all the teeth does not rid the pharyngeal lymphoid tissue nor the foci in chronic bronchitis of streptococci. Neither does antibiotic therapy have a lasting effect on these resident floras. In some patients, even persistent parenteral antibiotic treatment may not eradicate a "deep" streptococcus infection.

The search for foci and the "removal of foci" of infection, as diagnostic and therapeutic weapons, are controversial subjects. The majority of searches for foci about which so much has been said are superficial, to say the least. And most "removal of foci" mean little in the bacteriologic and immunologic economy of the host.

There should be no doubt, however, that apical dental infections inaccessible to antibiotics or to immunization are mechanical lesions requiring mechanical treatment. So also are scarred tonsils with focal abcesses, chronic empyema, and obstructive infections of the bowel. Chewing, swallowing, or straining pump these "foci." They should be corrected as a matter of prudent medicine.

There were four of 30 patients with one or another type of uveitis followed for 20 months or longer who benefited from this type of mechanical treatment. Three had teeth removed and one an infected colostomy stoma repaired. Four others had tonsils removed. One of these latter four did not respond until his prostate disease was recognized as the process to treat, following which he recovered. The other three have been well but the follow-up is still brief. These procedures can result in benefit to uveitis patients often enough to justify their serious consideration in the definitive treatment of obvious infections.

The course which other patients followed indicate that many unknown factors also contribute to the cause of uveitis. It is difficult to explain why some people develop uveitis, with no more than an apparently superficial infection as a possible cause. It is just as difficult to explain why other individuals with the most obvious septic processes can slough out their teeth, one by one, and never have any form of uveitis.

Some clue to the mechanism behind these paradoxes is gained from the repeated study of the delayed-type skin reactivity of these patients to bacterial products. Delayed-type reactivity fluctuates for known and unknown reasons. Its degree is associated often with specific eye symptoms. Further study of these relationships should be rewarding.

The second principle of management is to block the allergen immunologically if its source cannot be cut off. For this purpose, old tuberculin was used where tuberculosis was a likely cause. Streptomycin (1.0 gm., twice a day) and PAS (daily) were given to four patients in whom there was some suspicion of tuberculosis. One who had the least evidence for tuberculosis did not relapse. She had failed to respond to a previous course of old tuberculin injections. One patient with recurrent vitreous hemorrhages (Eales' disease) of two years' duration, who relapsed after streptomycin and PAS therapy, has now been symptom free for four years following the removal of an asymptomatic premolar tooth with an apical granuloma.

Old tuberculin was given to five other patients (six of 36 patients received old tuberculin), one of whom also received streptomycin and PAS. Only one of these did not relapse. He was the one person in the series with a strong family contact history. He developed recurrent retinal hemorrhages six months after his brother, whom he nursed, died of tuberculosis. He received old tuberculin only, and recovered. No re-

currence has been noted in a four-year follow-up period.

A course of brucellin injections was used in two patients. Both had recurrent retinitis. Both had recent exposures to raw milk. One had a ± reaction to brucellergin, but a positive brucella agglutination test (1:80) on two occasions. The other had negative brucella agglutination tests, but a markedly positive brucella skin test with a flare-up of eye symptoms at the time of the skin test. The first had a strongly positive tuberculin test. He received both old tuberculin and brucellin. The retinitis in both patients had not responded previously to full courses of the tetracycline compounds. Both cases of retinitis became quiescent coincident with desensitization treatment. Treatment was stopped. The one with the marked brucella cutaneous reactivities relapsed. The lesions have now been quiescent for 18 months coincident with a return to brucellin injections. No placebo controls have been run.

Bacterial vaccines were used in 17 of 36 patients. Seven of these vaccines were of the micrococcus family. The variable success with these has been described above. Six patients received β hemolytic streptococcus vaccine. No patients responded to this form of treatment. Three whose disease was probably due to a β hemolytic streptococcus infection seemed to respond to intensive penicillin therapy. The four other patients who received an α hemolytic streptococcus vaccine all relapsed even while on treatments.

The management of granulomatous uveitis is most difficult. Since the cause is present in the eye as well as elsewhere, antibiotic therapy would seem to be the ideal form of treatment. Sometimes this is successful.[44] More often, this therapy has been disappointing, particularly in tuberculosis of the eye.[45] Increasing immunity and diminishing hypersensitivity by appropriate injections may be successful.[46] It is apparent that reactions about living parasites within the optic tract are complex. The multiple antigens liberated from these areas can cause cell damage by means of various mechanisms, including the release of toxins, and the overlay of immediate and delayed allergic responses.

Most to be feared are explosive allergic responses which may be induced by inadvertent skin testing or exacerbations in other lesions in the host, since this may be followed by dissemination of the disease within the eye. On the other hand, there is a place for desensitization and immunization in these patients as holding procedures, even though they do not have the definitive effect they may have in nongranulomatous uveitis.

Conclusions

The preceding comments on the method of management of infections in patients with uveitis indicate how little we know about the cause of these conditions. Any conclusions which tempt the thoughtful person can be challenged. There are certain features of this body of information, however, which bear some re-emphasis:

a. The patients with uveitis in this small series had the same frequency of common allergic manifestation as is found in the population at large.

b. There was a frequent history of arthritis of some type among the selected chronic recurring types of uveitis of this series (30 percent).

c. The cutaneous responses of patients with uveitis to bacterial skin testing agents varied in degree, in time, and in type. Individuals often showed a marked reaction to one testing material and none at all to another. These degrees of reactivity were influenced by specific infections. Sometimes, increased cutaneous reactivity was coincident with flare-ups in eye disease. On many occasions, both skin and uveal reactivity fluctuated without apparent overt infectious causes.

d. Antibiotics, tuberculin therapy, bacterial vaccines, and removal of "foci of infection" are often unsuccessful in causing a remission in chronic or recurring uveitis.

From a strictly bacteriologic and immunologic point of view, eradication of infections by these means is rarely accomplished. Until more is known regarding the multiple factors which cause various types of uveitis, the prudent use of these therapeutic weapons may result in gains which justify their further exploration.

e. Indirect evidence from clinical observations and a consideration of basic mechanisms of allergic reactions support the view that nongranulomatous uveitis is most often a manifestation of a remote infection elsewhere in the host. Granulomatous uveitis may reflect the same variations in the allergic response of the host to its causative agent. It is a complex process which is much more difficult to manage.

Summary

1. Recent developments in the field of allergy are reviewed with reference to their role in the development of various inflammatory forms of eye disease. Particular attention is devoted to bacterial allergy.

2. A medical evaluation of 36 patients with various forms of eye disease referred to the internist for a search for foci of infection is presented.

3. One fifth of these persons, or the expected incidence in an unselected population, gave a past history of allergy. One third gave a past history of transient arthritis. Two patients had frank rheumatoid arthritis of mild degree. No patient had a past history of tuberculosis. Two patients only gave a history of tuberculosis contact.

4. Specific infections were related to one or more attacks of inflammatory eye disease in 16 patients as follows: Teeth, eight; pharynx, three; prostate, two; bowel, two; chronic empyema, one. Ten patients gave no epidermologic clues as to the cause of their eye trouble. The other 10 patients had various evidences of low-grade infections which were difficult to evaluate.

5. Skin tests done with a variety of antigens prepared from common bacteria, as well as with commercial preparations of tuberculin and brucellergin, were found to be useful.

6. The principles of medical management of these disorders is discussed.

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References

1. Koch, R.: Fortsetzung der Mitteilungen ueber ein Heilmittle gegen Tuberkulose. Deutsch. Med. Woch., **17**:101, 1891.

2. van Heuven, J. A.: Experimental corneal grafts. Am. Scientist, **41**:81, 1953.

3. Snell, A. C., Jr.: Ocular and subcutaneous inflammatory responses to transplantation of heterologous tumors. Arch. Ophth., **48**:298-306, 1952.

4. Woods, A. C., and Burky, E. L.: Experimental studies on ocular tuberculosis: VII. Effect of desensitization with tuberculin on experimental ocular tuberculosis. Arch. Ophth., **29**:369, 1943.

5. Elschnig, A.: Studien zur Sympathischen Ophthalmie: I. Wirkung von Antigenins vom Augeninnern aus. Arch. f. Ophthalmie, **75**:459, 1910; **76**:509, 1910; **79**:428, 1911.

6. Woods, A. C.: Allergy and Immunity in Ophthalmology. Baltimore, Johns Hopkins Univ. Press, 1933.

7. ———: Clinical and experimental observation on the use of ACTH and cortisone in ocular inflammatory disease. Am. J. Ophth., **33**:1325, 1950.

8. Follis, R. H., Jr.: Immunizing effect of old tuberculin on experimental tuberculous infection. Proc. Soc. Exper. Biol. & Med., **39**:45, 1938.

9. Ebert, R. H.: Development of tuberculous infection: In vivo observations in the rabbit ear chamber. Proc. Soc. Exper. Biol. & Med., **68**:625, 1948.

10. Drea, W. F., and Andrejew, A.: The Metabolism of the Tubercle Bacillus. Springfield, Ill., Thomas, 1953, p. 280.

11. Benacerraf, B., and Kabat, E. A.: A quantitative study of the arthus phenomenon induced passively in the guinea pig. J. Immunol., **64**:1, 1950.

12. Baldwin, E. R.: Studies in immunity to tuberculosis: I(a). Hypersusceptibility or anaphylaxis. J. Med. Research, **22**:189, 1910.

13. Zinsser, H., and Tamiya, T.: An experimental analysis of bacterial allergy. J. Exper. Med., **44**:753, 1926.

14. Zinsser, H., and Mueller, J. H.: On the nature of bacterial allergies. J. Exper. Med., **41**:159, 1925.
15. Bail, O.: Uebertragung der Tuberkulinempfindlichkeit. Ztschr. Immunitaetsforsch., **4**:470, 1909.
16. Chase, M. W.: The cellular transfer of cutaneous hypersensitivity to tuberculin. Proc. Soc. Exper. Biol. & Med., **59**:134-135, 1945.
17. Lawrence, H. S.: The cellular transfer of cutaneous hypersensitvity to tuberculin in man. Proc. Soc. Exper. Biol. & Med., **71**:516-522, 1949.
18. ———: The cellular transfer in humans of delayed cutaneous reactivity to hemolytic streptococci. J. Immun., **68**:158, 1952.
19. Rich, A. R., and Lewis, M. R.: The nature of allergy in tuberculosis as revealed by tissue culture studies. Bull. Johns Hopkins Hosp., **50**:115, 1932.
20. Rich, A. R.: The Pathogenesis of Tuberculosis, Springfield, Ill., Thomas, 1951, ed. 2.
21. Favour, C. B.: In vitro effect of tuberculin on cells. Bibliotheca Tuberculosa Separatum Fasc., **5**: 221, 1951.
22. Cruickshank, C. N. D.: Sensitivity to tuberculin. Nature, **168**:206, 1951.
23. Jacobi, F., and Marks, J.: On the tuberculin sensitivity of epithelial cells in vitro. J. Hyg., **51**:541, 1953.
24. Marks, J., and James, D. M.: The effect of tuberculin on sensitized and normal leucocytes. J. Hyg., **51**:340, 1953.
25. Kirchheimer, W. F., Hess, A. R., and Spears, R. G.: Attempts at passive transfer of tuberculin type of sensitivity with living granulocytes. Am. Rev. Tuberc., **64**:516, 1951.
26. Zinsser, H.: Studies on the tuberculin reaction and on specific hypersensitiveness in bacterial infection. J. Exper. Med., **34**:495, 1921.
27. Long, J. B., and Favour, C. B.: The ability of ACTH and cortisone to alter delayed type bacterial hypersensitivity. Bull. Johns Hopkins Hosp., **87**:186, 1950.
28. Favour, C. B.: In vitro uptake of tuberculin tagged with I^{131} by peripheral blood leucocytes. To be published.
29. Ritts, R., and Favour, C. B.: In vivo uptake of isotope-tagged tuberculin by leucocytes. To be published in J. Immunol.
30. Boyden, S. B.: Fixation of bacterial products by erythrocytes in vivo and by leucocytes. Nature, **171**:402, 1953.
31. Holst, P. M.: Studies on the effects of tuberculin. Tubercle, **3**:249, 289, 337, 1922.
32. Braude, A.: Personal communication.
33. Pappenheimer, A. M., Jr., and Williams, C. M.: The effects of diphtheria toxin on the cacropia silkworm. J. Gen. Physiol., **35**:727, 1952.
34. MacFarlane, M. G., and Knight, B. C. J. G.: The lecithinase activity of Cl. welchii toxins. Biochem. J., **35**:884, 1941.
35. Pillemer, L., Whittler, R., and Grossberg, D. B.: Isolation and crystalization of tetanal toxin. Science, **103**:615, 1946.
36. Burnet, F. M.: The exotoxins of staphylococcus pyogenes aureus. J. Path. & Bact., **32**:717, 1929.
37. Downie, A. W.: A comparison of the value of heat-killed vaccines and toxoid as immunizing agents against experimental staphylococcus infections in the rabbit. J. Path. & Bact., **44**:573, 1937.
38. Steinhaus, E. A.: Principles of Insect Pathology. New York McGraw-Hill, 1949.
39. Trager, W.: Intracellular micro-organismlike bodies in the tick dermacentor variabilis say. J. Parasitol., **25**:233, 1939.
40. Woods, A. C.: The diagnosis and treatment of ocular allergy. Am. J. Ophth., **32**:1457, 1949.
41. Harris, T. N., and Ehrich, W. E.: The fate of injected particulate antigens in relation to the formation of antibodies. J. Exper. Med., **84**:157, 1946.
42. Sarkies, J. V. E.: Ocular onchocerciasis. Brit. J. Ophth., **36**:81, 1952.
43. Parsons, H. E.: Nematode chorioretinitis: Report of case with photographs of viable worm. Arch. Ophth., **47**:799, 1952.
44. Favour, C. B.: Immunity. Transplantation Bull., **1**:145, 1954.
45. Adair, C. B., Drobeck, B., and Bunn, P. A.: Use of rabbit eye as a tissue to study tuberculosis: II. Effect of certain antituberculosis agents upon ocular tuberculosis. Amer. Rev. Tuberc., **64**:207, 1951.
46. Horne, H., and Macaskill, J.: Effect of para-amino-salycilic acid alone and in association with streptomycin on experimental ocular tuberculosis. Brit. J. Ophth., **35**:459, 1951.
47. Okell, C. C., and Elliott, S. D.: Bacteremia and oral sepsis, with special reference to etiology of subacute endocarditis. Lancet, **2**:869, 1935.
48. Glaser, R. J.: General principles of antibiotic therapy. J. Amer. Dent. A., **46**:129, 1953.
49. Birbeck, M. A., Buckler, W. St. J., Mason, R. M., and Tegner, W. S.: Iritis as the presenting symptom in ankylosing spondylitis. Lancet, **2**:202, 1951.
50. Favour, C. B., and Sosman, M. C.: Erythema nodosum. Arch. Internat. Med., **80**:435, 1947.
51. Siegal, S. S., and Suderman, T.: Latent atopy: An incidence of the atopic state. J. Allergy, **25**:20, 1954.

SPASM OF FIXATION*

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Fixation refers to a maintenance of the posture of the eyes by tonic contraction of the ocular muscles so that the retinal images of the object which is fixed fall upon the two fovea.

MECHANISM OF FIXATION

Fixation or more appropriately the act of "fixation and refixation" may be considered as consisting of two components—a *voluntary* cortical mechanism for coarse adjustment and an *involuntary* reflex subcortical mechanism for finer and more delicate adjustments.

HORIZONTAL VOLUNTARY MECHANISM

The voluntary[1] mechanism utilizes the pathways for conjugate lateral and vertical gaze. Movements for lateral gaze are probably initiated in the oculogyric center in the Betz cells of Brodman's area 8, alpha, beta, and gamma located in the posterior portion of the second prefrontal convolution. The fibers which arise in these cells pass through the corona radiata and enter the internal capsule. These fibers cross over to the opposite side in the midbrain and upper part of the pons. From here the assumption appears to be that the fibers enter the center for conjugate gaze probably situated in front of the sixth nerve nucleus near the midline. From this center fibers are probably distributed to the ipsilateral sixth nerve nucleus, while others cross the midline and ascend in the posterior longitudinal bundle to reach the third nerve nucleus, of the opposite side (fig. 1).

VERTICAL VOLUNTARY MOVEMENTS

As yet no cells have been identified in the frontal cortex, subserving the function of vertical conjugate movements. However, if the horizontal extraocular muscles are severed, vertical movements have been obtained by stimulation of the oculogyric center in the posterior portion of the second prefrontal convolution. Fibers for vertical gaze

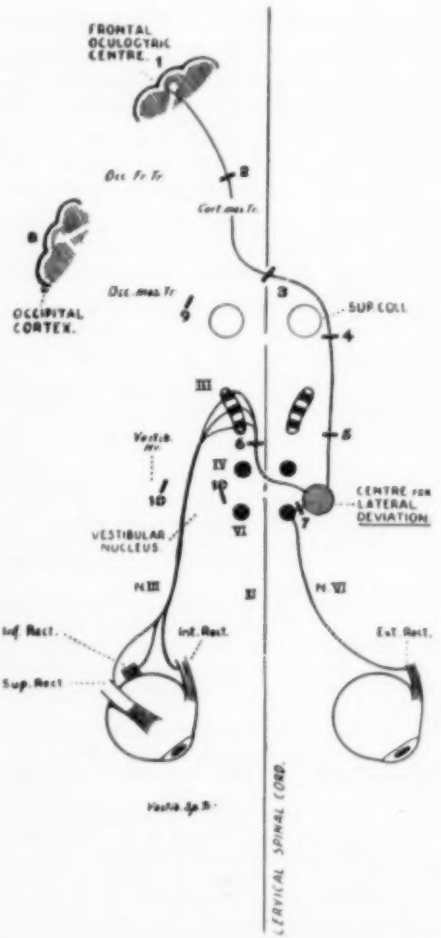

Fig. 1 (Alfano). The central organization for conjugate lateral gaze. (Modified after Duke-Elder.)

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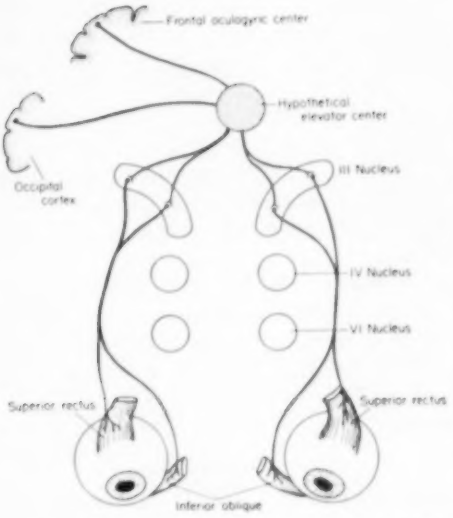

Fig. 2 (Alfano). The central organization for conjugate elevation of the eyes. (Modified after Duke-Elder, after Adler.)

have not been identified in the internal capsule. They have, however, been identified in the region of the superior colliculus and from here are believed by some authors to pass to a hypothetical elevator and depressor center just below the superior colliculus and from these centers probably enter the posterior longitudinal bundle to be distributed to the appropriate oculomotor nuclei as shown in Figures 2 and 3.

Involuntary (reflex) fixation

In speaking of the involuntary fixation reflex Alder[2] says:

"The centers and pathways for this reflex in man are not known with any certainty."

The afferent pathway is, without question, the visual fibers from the retina to the calcarine cortex (fig. 4). There is no agreement as to the layer of cells of the visual cortex in which the motor fibers begin. Most authors consider the cells of area 17 of Brodman as the beginning of the efferent arc, but Hines has given some evidence for believing that the optomotor pathway begins in the cells of area 18, the parastriate area, and 19, the peristriate area, rather than in the striate area itself.

From the optomotor area in or around the calcarine fissure, the fibers pass downward to the medial side of the visual radiation and through the posterior portion of the internal capsule to the basal ganglia and the lower conjugate centers. Spiegel and Sommer trace the fibers as follows:

"Starting from the optomotor zone surrounding the area striata, the fibers seem to pass under the angular gyrus and are observed in the lateral wall of the posterior end of the inferior horn of the lateral ventricle internal to the corticopetal optic fibers in the internal sagittal stratum. Further on they are found in the pretectal area and in the roof of the anterior corpora quadrigemina and the lateral geniculate body. From the rhombencephalon on, the corticofugal impulses apparently use the vestibular ocular reflex pathways to reach the eye muscles and finally reach the appropriate ocular muscles through the posterior longitudinal bundle."

The voluntary mechanism probably exerts

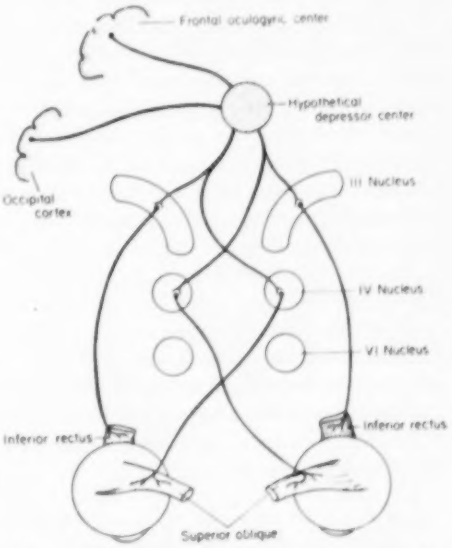

Fig. 3 (Alfano). The central organization for conjugate depression of the eyes. (Modified after Duke-Elder, after Adler.)

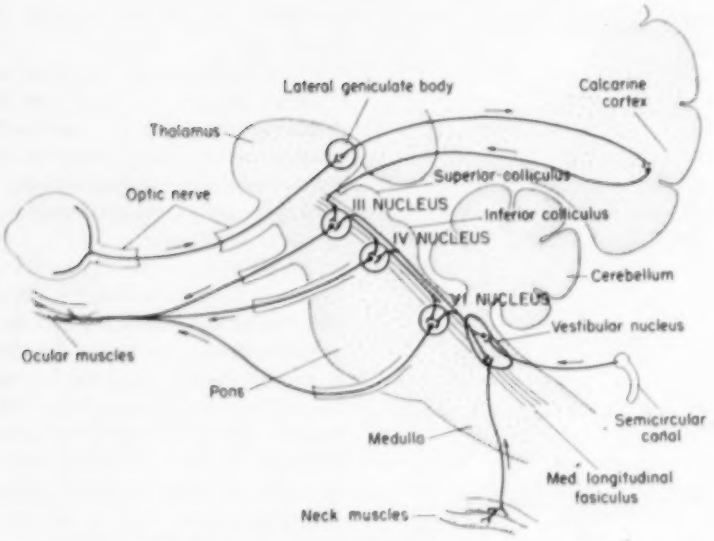

Fig. 4 (Alfano). Sagittal section showing reflex fixation pathway (after Adler).

an inhibitory influence upon the subcortical (reflex) mechanism.

Spasm of fixation

It appears that if the voluntary fixation mechanism is abolished or destroyed, an exaggeration and intensification of the reflex fixation mechanism may supervene with a resultant spasm of fixation. This fixation spasm is initiated and perpetuated by proprioceptic impulses from the ocular muscles themselves, resulting initially from the fact that retinal impulses are continually acting upon an uncontrolled cortical mechanism.

Characteristics

Spasm and intensification of the fixation reflex is usually associated with a paresis or paralysis of voluntary conjugate lateral or vertical movements and voluntary convergence, with a retention and intensification of the proprioceptive reflexes.

I. *Paresis or paralysis of voluntary conjugate lateral or vertical movements and voluntary convergence*

In a typical case the patient is unable to look to either side on command or to an object which he can see placed on either side of him, and upon attempting to do so, will usually turn his head in the direction in which he has been asked to look. At times he may be able to look to one or both sides by bringing his eyes over in a series or irregular, jerky movements which obviously requires much effort and is accompanied by evidences of distress in the patient such as jerking of the head, groaning, clenching of the fingers, and flexion and rotation of the body.

Although the patient is unable to turn his eyes on command or at will, his eyes may occasionally move, apparently involuntarily, in all directions as though to explore space around him.

There may be an associated paralysis of convergence, but more frequently although sudden convergence on a near object is not possible, if the gaze is fixed on a distant object, normal convergence may occur if the object is slowly brought near.

II. *Intensification of the fixation mechanism*

Although voluntary movements are im-

possible, the patient can follow an object which he has already fixed provided the object is moved slowly and uniformly. However, once the object has been fixed, in order to move the eyes so as to follow the object, the patient must first interrupt the fixation reflex. This he does by blinking, turning and jerking his head, or by placing his hand between his eyes and the object of his fixation. Blinking the eyes invokes the Bell's phenomenon and breaks fixation; following which a horizontal excursion occurs in the direction in which the object is being moved. Refixation now occurs, and, in order to continue the lateral excursion of the eyes, the same mechanism for breaking up the fixation spasm occurs.

III. *Retention of the proprioceptive reflexes*

Although the patient is voluntarily unable to move his eyes from side to side or up and down, full lateral or vertical excursions of the eyes may be obtained by passively rotating the head. For example, if the patient cannot turn his eyes to the left side, rotation of the head to the right causes passive deviation of the eyes to the left, for although his head is moved passively the eyes remain directed at the point upon which they were originally fixed. If the head is moved fast or jerkily, these compensatory ocular movements are probably mediated through labyrinthine reflexes, whereas if the movement of the head is slow they are probably mediated by proprioceptive reflexes from the neck muscles. These proprioceptive phenomena indicate that the oculomotor nuclei are functional and thus implicate a supranuclear mechanism.

In these cases, caloric stimulation of the labyrinth, instead of producing a typical nystagmus with a slow phase and a quick recovery phase, gives rise to a tonic deviation toward the side in which the slow phase of the nystagmus would be expected to occur. This deviation of the eyes resulting from labyrinthine stimulation may be suppressed if fixation is encouraged during the time the test is being performed but can be made to occur if fixation is embarrassed by placing a card before the eyes.

CASE REPORT

This six-year-old white boy was first seen at the Children's Memorial Hospital at the age of five years because he did not appear to move his eyes when looking at things on either side of him. This child was the first of the mother's two pregnancies. He was delivered at full time, and the labor was short and abrupt, lasting about four and one-half hours. No forceps were used in the delivery. During the third trimester of gestation the mother gained considerable weight which was thought to be due to a polyhydramnios. There was no postnatal cyanosis. The patient was born with an occipital meningocele which was removed at the age of one month. The child's development was apparently normal; however, the Stanford-Binet I.Q. rating was 73. Neurologic examination was negative except for some hypotonia of all the extremities and some difficulty in speech.

Laboratory studies, including urine, hemoglobin, red and white cell count, and serology were normal. Skull X-ray films showed a defect in the occipital bone in the midline as shown in Figure 5.

Eye history and examination. The mother stated that, when the baby was 16 months of age, she noticed that he had to turn his head from side to side to see things instead of moving his eyes. She felt that there may have been some improvement from the age of 16 months to five years, particularly during the last year. The visual acuity in the right eye varied from 20/70 to 20/40 and in the left from 20/70 to 20/30. There was a plus 2.25D. sph. refractive error in each eye. Pupils and fundi were normal. Peripheral fields showed a generalized contraction, undoubtedly functional, to the 10-degree circle using a 5.0- and 10-mm. white target.

Examination of the extraocular muscles revealed a preference for fixation with the

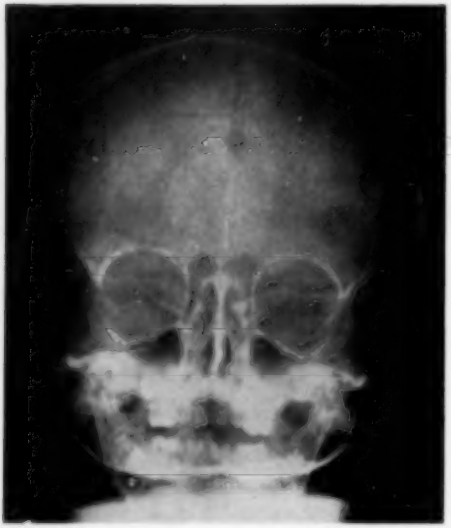

Fig. 5 (Alfano). Radiograph of skull, showing defect in occipital bone.

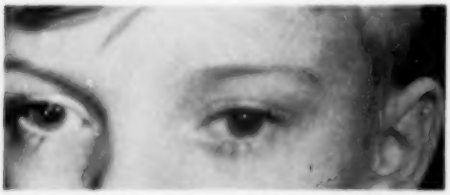

Fig. 6 (Alfano). Eyes in primary position.

Fig. 7 (Alfano). Normal upward gaze.

right eye. With the right eye fixing, the left eye was divergent about 10 to 15 degrees (fig. 6). Upward and downward gaze appeared normal (figs. 7 and 8). The patient could not look to either the left or the right on command or look at an object placed on either side of him, which he could see. In attempting to look to either side, the patient

Fig. 8 (Alfano). Normal downward gaze.

would instinctively turn his head or his head and shoulders to that side, instead of moving his eyes. There were no quick jerking movements of the head, however. When the patient's head was turned to the right by the examiner, there was full lateral excursion of the eyes to the left; upon turning the patient's head to the left, there was full lateral excursion of the eyes to the right (figs. 9 and 10).

If the patient were fixing an object in the primary position he could move his eyes

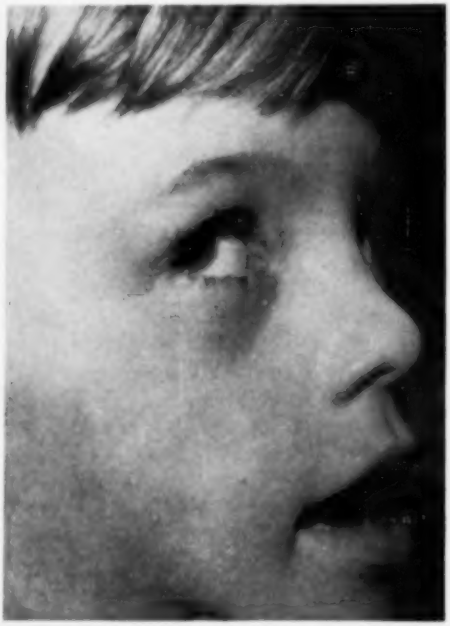

Fig. 9 (Alfano). Turning of the head to the left, producing conjugate deviation of the eyes to the right.

laterally by the following mechanism:

In moving from the primary position to the left lateral position, the patient would first blink (fig. 11) causing his eyes to turn upward, following which the eyes would be carried to the 25-degree mark on the perimeter; following this, another blink occurred, with a rolling up of the eyes and a tilting of the head backward. The eyes would then carry over to the 55-degree mark on the perimeter, at which position another blink occurred.

Having reached the left lateral position, the eyes could be carried from the left lateral to the right lateral position as follows:

The eyes were moved by a series of jerky movements from the left lateral to the primary position. At the primary position the patient would blink, the eyes would roll upward, and, he would tilt his head backward; the eyes would move 30 degrees to the right of the primary position. At this point another blink occurred and the eyes moved to about the 50 to 55-degree position on the perimeter, at which point another blink occurred.

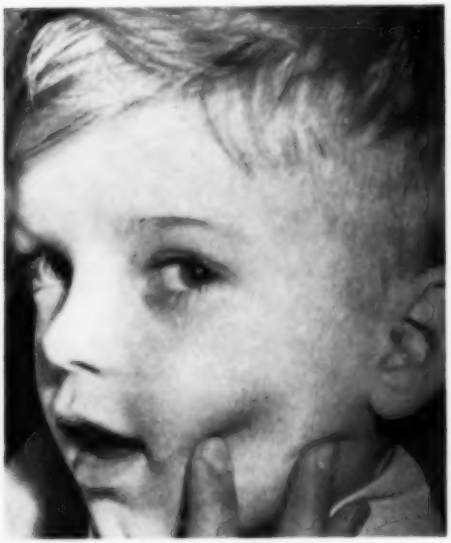

Fig. 10 (Alfano). Turning of the head to the right, producing conjugate deviation of the eyes to the left.

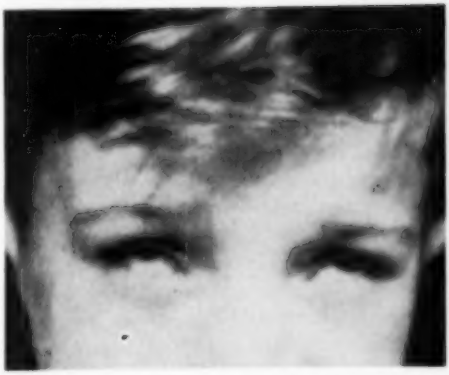

Fig. 11 (Alfano). Invocation of the blinking reflex with resulting deviation of the eyes upward (Bell's phenomenon) in order to break fixation and initiate conjugate lateral excursion.

Convergence was not possible. The patient was observed for one year, during which time some improvement seemed to occur.

Site of lesion

In his case report, Gowers[3] felt that the lesion was in the corpora quadrigemina. According to Holmes, [4,5] in the cases reported by Lutz and Tibing, there were bilateral injuries to the frontal oculomotor centers. Holmes,[4,5] however, felt that more often the projection fibers from the oculogyric centers were involved either in the internal capsule or caudal to it. He also felt that the lesion could result from a primary degeneration of the corticocollicular fibers and, in these cases, the condition could be familial and progressive, as in the cases reported by Von Pallathy, Ballet, Cantonnet, and Tagult.

Cogan[6] presented the case of a patient with an oculomotor apraxia who at times would show a spasm of fixation. The patient was believed to have had a postpartum thrombosis of the sagittal sinus.

In my case several factors of importance should be noted:

1. The patient had a meningocele or a meningoencephalocele in the occipital region. This condition is usually associated with atrophy of the underlying cortex and some dilatation of the ventricular system. There-

fore, it is possible that there may have been a defect in the occipital cortex or in the internal sagittal stratum due to pressure of a dilated ventricle on the corticofugal fibers as they pass from the optomotor area to the vestibular nucleus in the pons. However, while a lesion of this type would interfere with the involuntary fixation mechanism, it would in no way account for the paresis of conjugate gaze.

2. The patient was delivered after a short precipitous labor and the mother had polyhydramnios. According to Ford,[7] intracranial hemorrhage in infants who survive is usually venous in origin. Bleeding over the convexity of the frontal lobes, usually due to an overriding of the parietal bones, may be caused by tearing, either of the superior sagittal sinus or of some of the cerebral veins which empty into the superior sagittal sinus. Hemorrhage into the frontal cortex, involving the oculogyric centers in the frontal lobes, could easily account for paresis of lateral conjugate gaze. As a result of destruction of the voluntary frontal cortical centers for fixation, the involuntary subcortical mechanism would be uninhibited by the frontal cortical centers and an uncontrolled, involuntary fixation mechanism would lead to spasm of fixation.

In all probability, the spasm of fixation in the case presented was due to damage to the frontal oculoygyric centers which resulted from venous hemorrhage into the frontal lobes incident to the trauma of a precipitous delivery.

Summary

A case of spasm of fixation is reported in which the cause was thought to be damage to the frontal oculogyric centers resulting from hemorrhage from the superior sagittal venous sinus incident to birth trauma.

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References

1. Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby, 1949, v. 4, p. 4155.
2. Adler, F. H.: Physiology of the Eye: Clinical Application. St. Louis, Mosby, 1950, pp. 371-378.
3. Gowers, W. R.: Note on a reflex mechanism in the fixation of the eyeballs. Brain, **2**:39-41, 1879.
4. Holmes, G.: The cerebral integration of ocular movements. Brit. M. J., **2**:107-112, 1938.
5. ———: Spasm of fixation. Tr. Ophth. Soc. U. Kingdom, **50**:253-262, 1930.
6. Cogan, D. G., and Adams, R. D.: A type of paralysis of conjugate gaze: Oculomotor apraxia. Arch. Ophth., **50**:434-442, 1953.
7. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood, and Adolescence. Springfield, Ill., Thomas, 1944, ed. 2, pp. 187-190.

ELEPHANTIASIS NOSTRAS*

Report of a case

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Elephantiasis nostras or solid edema of the eyelids appears to be sufficiently rare, especially in the American literature, to justify reports of new cases. Pedraglia and Deutschmann[1] reported the first case in 1888, and Carletti[2] found only 22 cases reported in the interval up to 1924; since that time there have been several cases reported in the European literature. The most recent case reported in the American literature was by Beigelman[3] in 1932. The deformity is obvious, and is quickly noted by the observer on gross inspection.

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Definition

According to Menon,[4] the first and very good description of this disease was written

about 600 B.C. by Sushruta in India. This ancient author so named the disease because the involved extremity resembled in appearance and texture the limb of an elephant. Metas[5] defines elephantiasis as a progressive histopathologic state characterized by chronic inflammatory fibrosis and hyperplasia of the dermal and hypodermal tissue which is preceded by, and associated with, venous and lymphatic stasis. Bertwistle and Gregg[6] define true elephantiasis as a condition of hypertrophy and hyperplasia of the skin and subcutaneous tissue formed in a part affected by lymphatic and probably venous obstruction as a result of bacterial infection, most probably streptococcal.

Duke-Elder[7] places elephantiasis of the lids under the general classification of hypertrophies of the eyelids which may be caused by either diffuse neoplastic disease or chronic and recurrent inflammation. Elephantiasis nostras is included in the latter group.

Case report

A 59-year-old white man presented himself complaining of painless swelling of the eyelids of 11 years' duration. The history revealed that the swelling had originally been intermittent with exacerbation of chronic inflammation characterized by diffuse injection of the lids. The patient had always resided in the northeast section of the United States.

During the past five years, the swelling had been constant with little evidence of inflammation. Four years prior to his admission to the Temple University Hospital, the patient was studied at another hospital, during which time the posterior cervical and auricular lymph nodes were biopsied. The histologic examination of the nodes revealed a chronic inflammatory reaction. For one year preceding the present admission, the patient had had difficulty in reading because his swollen lower lids obstructed vision through his bifocal segments.

Physical examination revealed a bilateral nonpitting edema of the upper and lower lids causing the latter to protrude two cm. from the face (fig. 1). The epidermis of the lids was thickened, mottled, and discolored. There was a slight rubor over the superciliary ridges. The visual acuity with correction was 20/20 bilaterally. The anterior and posterior cervical lymph nodes were barely palpable.

The results of laboratory procedures, including a hematologic survey, routine blood chemistry and serology, and X-ray studies of the teeth, chest, and paranasal sinuses, were all within normal limits.

At the time of operation, the infraorbital nerve as it emerged from the infraorbital canal was anesthetized with two-percent lidocaine hydrochloride (Xylocaine). A crescent-shaped incision was made five mm. below the inferior palpebral fissure, and as much of the redundant skin and subcutaneous tissue as deemed feasible was excised. The skin margins were carefully approximated with interrupted sutures. Identical procedures were carried out on the lower lids of both eyes.

A pressure dressing was applied, and the sutures were removed on the fifth postoperative day. This operation was identical with the procedure described by Heintz.[8]

Immediately postoperatively there was an ectropion of the right lower lid (fig. 2). The patient was instructed to massage his lower lids with cocoa butter. Six weeks following the operation, the patient was pleased with the cosmetic result (fig. 3). There was a concomitant reduction in the degree of edema of the upper lids, and the postoperative ectropion of the right lower lid had disappeared.

Photomicrographs of the excised tissue were made. Under low power (× 32, fig. 4), prominent fibrosis with obliteration of the subcutaneous fat is seen. The overlying epithelium reveals areas of both hypertrophy and atrophy with flattening of the rete pegs. Minimal hyperkeratosis with keratic follicular plugging is present. Scattered throughout are numerous lymphocytic channels,

Fig. 1 (Bobb). Preoperative appearance.

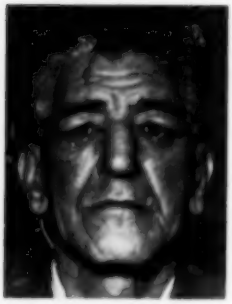

Fig. 2 (Bobb). Fifth postoperative day.

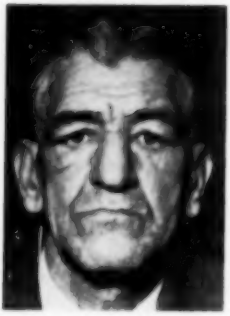

Fig. 3 (Bobb). Six weeks following surgery.

which on higher power ($\times$ 186, fig. 5) show proliferation with the formation of abundant endothelial channels. The fibrous stroma is edematous and infiltrated predominantly by lymphocytes with occasional plasma cells and macrophages. The inflammatory cells tend to aggregate about lymphatic and vascular channels as well as about skin appendages.

Fig 4 (Bobb). Low-power ($\times$32) photomicrograph revealing atrophy of epithelium with prominent fibrosis of subcutaneous tissues.

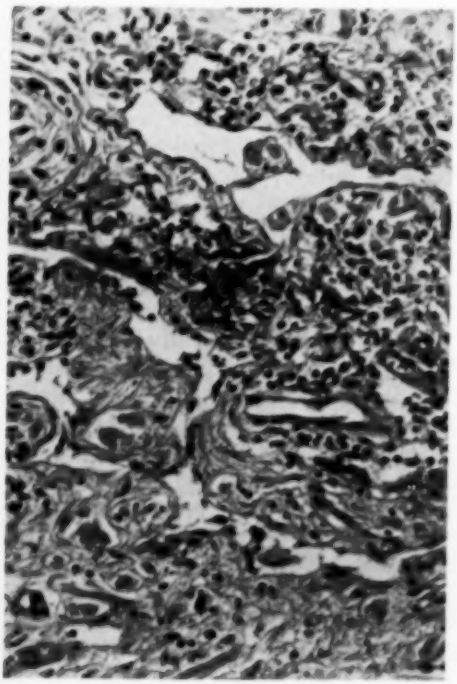

Fig. 5 (Bobb). Higher-power ($\times$186) photomicrograph, revealing cellular infiltration and many endothelial channels.

Etiology

Bacterial infection plays an important role in the etiology of nontropical and non-neoplastic elephantiasis of the lids. Grom's[9] case was that of a 14-year-old girl whose father had a severe case of erysipelas. Both of Heintz's[8] cases presented histories of streptococcal infection. Beigelman[3] stressed trachoma as a possible etiologic agent. Andersen's[10] case was that of a farmer who had a long history of eczema of the eyelids.

Keidan[11] reported the case of an eight-year-old girl who developed an acute bilateral inflammation of the eyelids three weeks following a traumatic hematoma on the forehead. The inflammation underwent periods of exacerbations and remissions. Bacteriology revealed a hemolytic streptococcus as the predominant organism. Penicillin rapidly dissolved all signs of inflammation; however the lid edema persisted with elephantoid changes developing clinically.

The evidence in the literature points to the fact that the elephantoid state does not arise from a single mechanical obstruction of the lymphatic and venous channels but is dependent upon infection with a resultant derangement of those structures.

In general, elephantiasis of the lids may be caused by diffuse neoplasia, most commonly neurofibromatosis (elephantiasis neuromatodes), hemagiomas (elephantiasis telangietodes), lymphangiomas (elephantiasis mollis), or leukemia. It may also be caused by recurrent inflammatory conditions as seen in the leonine overgrowths in nodular leprosy (elephantiasis graecorum), or the extension of leishmaniasis to the eyelids (elephantiasis leishmaniana) from the nose. The parasite, filaria bancrofti, which is by far the commonest cause of elephantiasis of an extremity, rarely causes this disease in the eyelids.

Diagnosis

Simple lymphedema of the eyelids may be caused by an infinite variety of local and systemic diseases. A few common causes of transient edema are hordeolum, acute chalazion, insect bite, orbital cellulitis, and angioneurotic edema. The common causes of persistent edema of the eyelids would include cardiac, renal, and hepatic disease, severe anemia, allergy, both hyper- and hypothyroidism, dermatitis medicamentosa, and chronic orbital infection. Pitting on pressure which occurs in simple lymphedema, but not in true elephantiasis, is a useful sign which may be used to differentiate the two diseases.

Elephantiasis can be differentiated from blepharochalasis (ptosis atrophica) when the latter is clearly defined as a disease of the upper eyelids characterized by atrophy and relaxation of the skin and supporting tissues of the eyelids, and due to chronic or recurring edema of the anterior orbital structures. In an extensive review of the literature, Alvis[12] found that the onset of blepharochalasis occurred before the age of 10 years in a third, and between the ages of 10 and 20 years in half the cases reported.

Steckler[13] discusses the etiology of "baggy eyelids." Herniation of fat through a weak septum orbitale, and epiblepharon, a rare congenital anomaly characterized by a horizontal fold of skin which covers the margin and lashes of the lower lid, must be considered in the differential diagnosis of elephantiasis.

Elephantiasis caused by a tumor is suggested when the skin can be raised in a fold or if circumscribed tumefaction is present.

In obscure cases, a soft tissue roentgenogram of the lids reveals an extensive network of trabeculation, representing advanced subcutaneous fibromatosis. According to Reichert[14] such trabeculation is not seen in simple lymphatic or vascular edema. The X-ray film is easily inserted between the lids and the eyeball so that roentgenograms are readily obtained, although they are rarely needed to make a positive diagnosis.

Treatment

Treatment is aimed at the correction of constitutional disorders, removal of septic

foci, and improvement of the general hygiene of the patient. These measures may stop the inflammatory process, and with it the progressive deformity of the lids. It is obvious, however, that the fibrous tissue already formed can best be removed only by surgery. The type and extent of the surgical procedure must be determined in each individual case. The injudicious removal of tissue near the lid fissure may cause an ectropion as was seen in the right eye of the present case. In 1933, New and Kirch[15] reported excellent cosmetic results in the treatment of elephantiasis of the face by the injection of boiling water into the involved tissue. This therapy is not advised for elephantiasis of the eyelids.

In 1951 Andersen and Asboe-Hansen[10] reported a case of elephantiasis nostras involving the face and eyelids. They found that the involved tissue contained a mucopolysaccharide having a high content of hyaluronic acid. They theorized that the hyaluronic acid combined with cellular fluid to initiate fibroblastic proliferation. The patient was given a course of adrenocorticotrophic hormone. By means of repeated assays following the hormone therapy, it was shown that the hyaluronic acid content of the tissue was reduced. In the case reported, surgery was still required to correct the deformity of the lids. It is conceivable, however, that, if steroid hormone therapy had been given to the patient early in the disease, surgery would not have been required.

Summary

A case of elephantiasis nostras of the eyelids was presented and the clinical and pathologic aspects of this disease were outlined. This is believed to be the second such case reported in the American ophthalmic literature on this subject. The etiology, differential diagnosis, and treatment of the deformity were reviewed.

346 North Fifth Street.

References

1. Pedraglia and Deutschmann: Chronisches Lidödem bei erisipelas-artiger Entzundung mit Tumorenbildung an der Lidrandern. Arch. f. Ophth., **34**:161, 1888.
2. Carletti, P.: Elefantiasi delle palpebre. Rome, Tipografia Ditta Ludovic Cecchini, 1924.
3. Beigelman, M. N.: Elephantiasis of the eyelid. Arch. Ophth., **8**:218-225 (Aug.) 1932.
4. Menon, T. B.: Problem in filariasis (Maharaja of Travancore Curzon Lectures, University of Madras.) Madras, Thompson and Co. Ltd., 1935.
5. Matas, R.: The surgical treatment of elephantiasis and elephantoid states dependent upon chronic obstruction of the lymphatic and venous channels. Am. J. Trop. Dis., **1**:60, 1913.
6. Bertwistle, A. P. and Gregg, A. L.: Elephantiasis. Brit. J. Surg., **16**:267 (Oct.) 1928.
7. Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby Co., 1952, v. 5, pp. 4993-4998.
8. Heintz, M. A.: Eléphantiasis des Paupières. Bull. Soc. belge ophtal., **87**:147, 1947.
9. Grom, E.: Elephantiasis of the eyelids. Tr. Ophth. Soc. U. Kingdom, **68**:255, 1948.
10. Andersen, S. R., and Asboe-Hansen, G.: Elephantiasis of the face: A report of a case treated with ACTH. Acta Ophth., **29**:487-498, 1951.
11. Keidan, S. E.: Elephantiasis nostras. Lancet, **1**:79-80 (Jan.) 1954.
12. Alvis, B. Y.: Blepharochalasis: Report of a case. Am. J. Ophth., **18**:238-246 (Mar.) 1935.
13. Steckler, M. I.: Baggy eyelids. Am. J. Ophth., **37**:113-115 (Jan.) 1954.
14. Reichert, F. L.: The recognition of elephantiasis and elephantoid condition by soft tissue roentgenography. Arch. Surg., **20**:543 (Apr.) 1930.
15. New, G. B., and Kirch, W. A.: Permanent enlargement of the lips and face. J.A.M.A., **100**:1230-1233 (Apr.) 1933.

NOTES, CASES, INSTRUMENTS

EFFECT OF VERSION AND VERGENCE MOVEMENTS ON OCULAR TORSION*

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New York

An interesting feature of the ocular movements is that the orientation of the retinal meridians of the moving eye depends partly on the nature of the associated movement of the other eye.

We must start with a few definitions and restate a few well-established facts. Version movements are movements of both eyes in the same direction. Vergence movements are movements of both eyes in opposite directions as in convergence and divergence.

The primary position of the eyes for distant vision is the position the eyes assume when looking straight forward in a horizontal plane. The distinguishing characteristic of this position is that movements from this position straight up, down, right, or left are free from torsion. We can think of torsion for the present merely as an inclination of the normal vertical, horizontal, and other meridians of the eye, without regard as to cause or manner.

Version movements in an oblique direction, say, up and to the left, or up and to the right, are accompanied by torsion, sometimes called false torsion. The important fact is that there is a tilting of the meridians of each eye. In looking up and to the left both eyes undergo some levotorsion, which is intorsion of the right eye and extorsion of the left eye. Looking down and to the left, both eyes undergo dextrotorsion, that is, extorsion of the right eye and intorsion of the left eye.

TORSION ON CONVERGENCE

Now, whereas, in oblique version movements with fixation at six meters, the torsion of the two eyes is symmetrical, that is, dextrotorsion or levotorsion of both eyes, we find a different state of affairs during convergence. When from the primary position for distance the eyes converge to some point in the horizontal plane there is some extorsion of each eye, that is, there is dextrotorsion of the right eye and levotorsion of the left eye. At a reading distance of 33 cm. (three meter angles of convergence) each eye is extorted about one degree. The extorsion increases with increasing convergence. Thus for a 12.5 cm. distance (about eight meter angles) the extorsion is about 2.5 degrees for each eye. For extreme convergence, say, for 8.0 cm. (about 12 meter angles) the extorsion is about four degrees for each eye.

This is the extorsion on convergence found in the horizontal plane. It seems to diminish as the plane of regard is lowered. Thus when the eyes are depressed 30 to 45 degrees below the horizontal, moderate convergence is free from all torsion. Helmholtz called this the primary position for convergence. When the eyes are depressed still more there is a slight *in*torsion of each eye.

However, when the eyes are raised above the horizontal, the extorsion on convergence increases. Thus when the eyes converge to a point in the median line, some 12 cm. away and 20 degrees above the horizontal, each eye is extorted about five degrees. In this position the angle of convergence is some 30 degrees and each eye converges 15 degrees. Note that in this position of elevation and convergence the right eye is turned 20 degrees up and 15 degrees to the left; the left eye is turned 20 degrees up and 15 degrees to the right.

Now when the eyes from the primary position make a version movement to fixate a point at six meters 20 degrees up and 15 degrees to the left, there is some levotorsion of *each* eye, say one degree of levotorsion. The point up and left which the eyes are

* Presented at the December 20, 1954, meeting of the Section of Ophthalmology of the New York Academy of Medicine.

made to fixate may be placed on an extension of the visual axis of the right eye as it is directed 20 degrees up and 15 degrees to the left in the act of convergence.

But in this strongly converged position the right eye is extorted. We see here that a movement of the right eye 20 degrees up and 15 degrees to the left may be accompanied sometimes by intorsion, sometimes by extorsion. When this direction of gaze is attained by a version movement with fixation at distance it is accompanied by intorsion. When this direction is attained by a vergence movement with fixation at near, it is accompanied by extorsion.

This change in the right eye from intorsion to extorsion while maintaining the same visual direction is an expression of a true torsion movement since it is a rotation around the visual axis. There is intorsion when fixating the distant target 20 degrees up and 15 degrees to the left in a version movement and extorsion on fixating a point at near lying on its own visual axis by a convergence movement of the left eye.

The change in the right eye from intorsion to extorsion when changing fixation from far to near is of course reversed to a change from extorsion to intorsion when changing fixation from near to far.

The mechanism for this reversal of torsion is rather difficult to explain. It may perhaps be explained in the illustration chosen by an increased effectivity of the medial rectus. Recent work has shown that when the eye is directed up this muscle has secondary actions, namely, elevation and extorsion. The extorting effect of the right medial rectus which increases with greater convergence, more than overcomes the intorting effect of the right superior rectus.

The same analysis, of course, can be applied to the other muscles in other directions of the gaze. Slight modifications have to be made in fixation below the horizontal.

We saw that when the eyes converge in the horizontal primary plane, there is a slight extorsion of both eyes which increases as convergence increases. The extorsion in convergence also increases as the eyes are raised, and decreases as the eyes are lowered. At some angle below the horizontal it becomes zero. This zero position varies with different observers. Helmholtz gave it as 45 degrees below the horizontal, and called it the primary plane for convergence. When the eyes are converged in a plane still lower, there is some slight *in*torsion of both eyes.

When from the primary position the eyes look at a distant object situated obliquely, say, down and to the left, the retinal meridians of both eyes are dextrotorted. The right eye is extorted, the left eye is intorted. Taking the right eye to illustrate the point we will say that the extorsion of the right eye is explained by the predominant extorting effect of the right inferior rectus, and the lessened intorting effect of the right superior oblique in this part of the field. But if the right eye is turned down and to the left to the same extent in an act of convergence, we find that the extorsion of the eye may become zero, in the so called primary plane for convergence, and may even change to intorsion.

This transformation of extorsion in a version movement to *in*torsion in a vergence movement may also be explained by the greater effectivity of the secondary torsion effect of the right medial rectus. When the eyes are lowered, the medial rectus helps the right superior oblique in its downward and intorting effect. This increasing intorting effect tends to neutralize or even to reverse the extorting effect of the right inferior rectus. The amount and type of torsion under different conditions varies widely with different observers and different experimenters. The figures given here are more or less average figures.

Summary

Torsion of the eyes takes place on version movements in oblique directions and on convergence. But they are different kinds of torsion. When for example the visual axis

of the right eye is directed up and to the left in a version movement with fixation at distance the right eye is intorted. But the same direction of gaze when associated with convergence and fixation at near is accompanied by extorsion. The secondary action of the medial rectus is suggested as the mechanism causing this reversal of torsion.

41 West 96th Street (25).

NEW CALIPER FOR OPHTHALMIC SURGERY*

RAMÓN CASTROVIEJO, M.D.
New York

In February, 1949, Mr. H. W. Matalene, Jr., of E. B. Meyrowitz, Inc.,† New York City, following my design, manufactured a caliper for making measurements on the eye, mainly for use in muscle surgery but also suitable for measuring and marking distances for scleral operations in retinal detachment and for plotting in the sclera the projection of retinal rents and of intraocular foreign bodies.

The new caliper was illustrated for the first time in a Meyrowitz Bulletin in April, 1949. The widespread acceptance of this simple instrument during the past six years has proven its usefulness and justifies my reporting it now.

The instrument has the following characteristics. The spread of the points of the caliper is regulated with the aid of a screw. A scale which can be read on either side is calibrated to measure in millimeters at the marking points. The first caliper made could measure only 15 mm.; recent ones read to 20 mm.

A moderate pressure on the sclera with the points leaves a mark which remains visible long enough to use whichever instrument is required, needle, knife, and so forth. If it should be required for the markings in the sclera to last longer than those made by the simple pressure of the points of the instrument, it may be obtained by dipping the points of the caliper in gentian violet. In a model of this instrument made by John Weiss, London, England, grooves extending along the arms of the caliper to the marking points can be filled with gentian violet, thus providing a way of leaving stain marks on the sclera upon contact with the points of the instrument.

* From the Departments of Ophthalmology, St. Vincent's Hospital, New York Eye and Ear Infirmary, and New York University Postgraduate Medical School.

† In addition to E. B. Meyrowitz, Inc., 520 Fifth Avenue, New York City, the caliper is manufactured by:

Storz Instrument Company, 4570 Audubon Avenue, St. Louis 10, Missouri.

V. Mueller & Company, Van Buren and South Honore Streets, Chicago 12, Illinois.

Maison Luer, 104 Boulevard Saint Germain, Paris 6, France.

John Weiss & Son, Ltd., 287 Oxford Street, London W. 1, England.

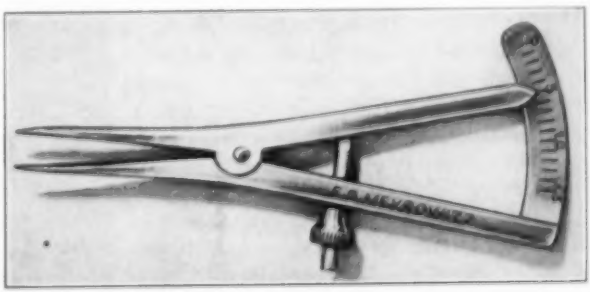

Fig. 1 (Castroviejo). A new caliper for ophthalmic surgery.

PARINAUD'S SYNDROME*

FROM OBSTETRIC TRAUMA WITH RECOVERY

JAMES E. LEBENSOHN, M.D.
Chicago, Illinois

A female infant, the firstborn of young parents (father, aged 25 years; mother, aged 21 years) was first seen when eight weeks old. The parents reported that since birth the eyes were constantly in a downward position while awake, though the globes turned up when asleep. The pediatrician found the child otherwise quite healthy.

Examination elicited reflex conjugate movements in all directions but upward. The pupils were dilated, gave no reaction to light, but constricted on convergence. The upper eyelids were extremely retracted (fig. 1). With passive turning of the head downward, the eyeballs rolled up, an action likened by Cogan[1] to that of a mechanical doll. The ophthalmoscope revealed no pathologic condition in the media or fundi.

The obstetrician communicated that delivery had required low forceps and rotation.

At the age of 17 months the infant had gained completely the ability to move the eyes upward and the upper lids were no longer retracted. The pupils were still dilated and unresponsive to light. Exposure to sunlight resulted in evident dazzling and tearing. By the following year the pupils were of usual size, and reacted to light; and the eyes appeared and behaved normally in all respects (fig. 2).

Since then, the parents have had another child, delivered without instrumental aid and free from any defect, ocular or otherwise. Both parents have compound myopic astigmatism, but no other ophthalmic abnormality. The correction of the mother is: R.E., −1.25D. sph. ⌒ −0.25D. cyl. ax. 85°, 20/13; L.E., −0.5D. sph. ⌒ −1.0D. cyl. ax. 80°, 20/13; that of the father is: R.E., −0.25D. sph. ⌒ −2.0D. cyl. ax. 105°, 20/15; L.E., −0.75D. sph. ⌒ −0.75D. cyl. ax. 75°, 20/15.

Fig. 1 (Lebensohn). Infant, aged eight weeks. Note retracted lids, dilated pupils, and position of eyes.

Duke-Elder[2] remarks that paralysis of vertical movements "indicates with considerable exactitude a lesion, hemorrhagic, neoplastic, or degenerative, in the subthalamic or upper peduncular region in front of the

Fig. 2 (Lebensohn). Child at age of two and one-half years. Lids, pupils, and position of eyes are now completely normal.

* From the Department of Ophthalmology, Northwestern University Medical School.

corpora quadrigemina and near the posterior commissure. With the loss of elevation there is not uncommonly a retraction of the upper lid and sometimes disturbances of the pupillary reaction."

Cogan[1] states that the corticofugal fibers for vertical gaze pass from the internal capsule via the brachia and superior colliculi to the third and fourth nuclei of the same and opposite sides. Destruction of the superior colliculi abolishes the vertical component from occipital excitation though not affecting apparently vertical movements from frontal stimulation. A lesion that extends no lower than the level of the posterior commissure isolates the ocular motor nuclei from cerebral incitation though the ocular motor nuclei remain intact.

In discussing such supranuclear lesions, Gordon Holmes[5] suggested that the distinction between upper and lower motor neurone paralysis could be applied profitably to ocular movements. It would seem that the spastic lid retraction that frequently accompanies paralysis of upward gaze could be explained on this basis. In the waking state the levator is tonically contracted and with the suppression of inhibitory impulses an exaggerated stretch reflex becomes manifest.

The first synapse of the pupillary light reflex is localized in the pretectal area (border of thalamus and superior colliculi), close to the supranuclear pathway for upward gaze, on which account an associated functional impairment is frequent.

Walsh[6] considers that dilated, fixed pupils usually precede the supranuclear paralysis of upward gaze. Walsh[6] has observed several instances of a transient Parinaud's syndrome of vascular origin. "One such case, seen through the courtesy of Dr. Benjamin Rones, exhibited total inability to elevate the eyes during a period of seven days when there was pronounced retraction of both upper lids. These signs disappeared suddenly and during the entire episode there had been no other complaint, and the patient seemed quite healthy."

Parinaud's syndrome as a sequel to head injury occurs rarely and is then usually associated with other involvement. Occasionally, however, a traumatic head lesion is remarkably localized so that, for example, ophthalmoplegia interna alone has followed. Duke-Elder[3] thinks that in such instances "the momentum of the blow may set up a wave of fluid in the third ventricle which breaks with its greatest force around the anterior end of the aqueduct of Sylvius . . . causing edema and petechial hemorrhages."

A thorough search of the literature has failed to disclose a case similar to that reported.* The child, now aged seven years, has normal upward motion of the eyes in movements of reflex fixation, following, and command as well as in counter-rotation of the head. Her experience happily illustrates the last as well as the first part of Duke-Elder's comment[4] that "entering this world is a difficult and dangerous adventure—almost as dangerous as living in it. It is; but it is to be remembered that most of the scars thus sustained are transient."

4010 West Madison Street (24).

*The following two more complex cases, however, might be of a like type. A. S. Breakey ("Ocular findings in cerebral palsy," Arch. Ophth., **53**: 852-56 [June] 1955) found one case of paralysis of upward gaze in 100 unselected children with cerebral palsy. This patient was in the dyskinesic group (with lesions in the basal ganglia). T. R. Hedges, Jr., and F. H. Adler ("Oculomotor manifestations of certain lesions in the brain stem," Arch. Ophth., **54**:141 [July] 1955) cite one case with complete loss of vertical movement associated initially with a transient left hemiparesis. The patient recovered upward and downward following movement. But command movement in upward gaze remained absent for two and one-half years. The authors attribute the cause of the Parinaud's syndrome in this instance to a vascular lesion.

References

1. Cogan, D. G.: Neurology of the Ocular Muscles. Springfield, Ill., Thomas, 1948, chap. VI.
2. Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby, 1949, v. 4, p. 4163.
3. ———: Ibid, p. 4125.

4. ——— : Ibid., 1954, v. 6, p. 5728.
5. Holmes, G.: Observations on ocular palsies. Brit. M. J., **2**:1165, 1931.
6. Walsh, F. B.: Clinical Neuro-ophthalmology. Baltimore, Williams & Wilkins, 1947, p. 306.

A FOCUSING ATTACHMENT FOR CLOSE-UP PHOTOGRAPHY

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San Antonio, Texas

When taking pictures of the eye at close range, the depth of field is quite limited. Most cameras, except those using groundglass focusing, depend upon fixed focus framing devices which are placed in the orbital area to be photographed with more hope than accuracy. As a result, many of the monocular photographs have the cilia in sharp focus when it was an iris lesion that should have been clear. Lateral pictures of the eye are particularly difficult when frames are used. There is a definite need for an accurate means of getting a lesion into sharp focus and occupying the center of the picture at the same time.

The principle of the attachment herein described is the crossing of two beams of light at about right angles to one another at a point in the center of the field and at a distance of sharpest focus for the camera's lens system. As the camera is brought toward the eye, two spots of light approach one another and, at the point of exact focus, they become one spot. If the camera is brought even closer to the eye the single spot again becomes two separate spots.

From Figure 1 it will be noted that the light sources are ordinary pen lights solidly mounted to metal posts attached to an aluminum plate on the bottom of the camera. Each light may be raised, lowered, or rotated—then locked in position by means of a bolt passing horizontally through the aluminum plate. A portion of the bulb filament is focused as a beam by a small lens and two pinhole diaphragms in a tube attached in front of the bulb. These particular penlights have rotary switches posteriorly placed.

Fig. 1 (Nisbet). A focusing attachment for close-up photography.

A testing screen is attached to the aluminum base in front of the camera. Prior to taking each picture it may be noted, as soon as the penlights are turned on, whether or not the light spots appear as one on the center of the screen. If they do not, an adjustment may be made after which the testing screen is removed and the picture taken.

Although it has no relation to the focusing device, there is a cylinder (fig. 1) with a closed end covering the Strobe light tube. There is a hole in its wall through which the flash from the lower side of the tube may pass to strike a plane mirror mounted at an angle. The light is reflected directly over the camera lens to the eye. In this way maximum lighting is obtained, the camera diaphragm opening may be reduced, and greater depth of field obtained.

The apparent inconvenience of verifying the focus prior to taking each picture or series of pictures is really unimportant in comparison to the accurate results obtained by photographing an eye at close range.

700 South McCullough.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

YALE UNIVERSITY CLINICAL CONFERENCES

January 7 and 28, 1955

DR. R. M. FASANELLA, *presiding*

PROCEDURE FOR CATARACT EXTRACTION

DR. GEORGE CORCORAN, JR., M.D., Springfield, Massachusetts, in a talk illustrated by a colored motion picture, gave a very lucid presentation of his procedure for cataract extraction. Several unusual features were discussed in detail:

1. The use of two cc. of 10-percent novocaine with adrenalin and hyaluronidase for retrobulbar injection, combined with massage of the eyeball for five minutes thereafter, as used by Chandler, to enhance akinesia and get a softer globe. A No. 20 needle is used with the tip sand-papered to dull it.

2. Complete iridectomy and direct zonular stripping from above, with lens sliding upward. Dr. Corcoran emphasized layer-by-layer stripping of the zonule.

3. The use of as many corneoscleral sutures (average six or seven) as necessary until the wound cannot gape when tested by pulling on a limbus-based conjunctival flap. The attempt is made to place sutures superficially—one-third to one-fourth of the corneal thickness—with a narrow bite near the edge; they are tied as tightly as possible so that they will slough out by themselves in one to three weeks. It would seem that this overcomes the reluctance to use more sutures because of the difficulty of removing them safely later.

Dr. Corcoran does not patch the unoperated eye, and has no hesitancy in getting the patient out of bed the day of surgery. When Chlorpromazine is used preoperatively, because of its occasional hypotensive effect, the patient is kept in bed one day. He has noted no evidence of visual toxicity from the use of 10-percent novocaine in the retrobulbar injection.

Discussion. DR. ERNEST ROSENTHAL: How long does the hypotony persist after operation?

DR. CORCORAN: For a few hours; no longer than with other methods.

DR. WILLIAM GLASS: How do your results with this procedure compare to other methods in regard to postoperative hyphema, vitreous loss, and reformation of the anterior chamber?

DR. CORCORAN: It is difficult to compare statistics except with large series of cases which have been completely analyzed and unselected. Other surgeons' reports include six percent (Kirby) and 2.9 percent (Hill). In the last 100 cases (except those with severe uveitis which all other series also exclude), there has been a two-percent vitreous loss.

There have been two-percent ruptured capsules where something was left in the anterior chamber. Additional capsules were ruptured but I have no hesitation in working over the hyaloid under direct vision to remove retained capsule. The incidence of postoperative hyphema, omitting cataracts secondary to uveitis, has been four to five percent; others report 2.6 percent to 21 percent. I think a knife section gives hyphema postoperatively.

There was only one iris prolapse, in a patient who fell out of bed on the 10th day at home. Hill reports 4.9 percent. The anterior chamber was reformed on the first postoperative day in 97 percent; the same as Hill reported. Late collapse of the anterior chamber has been about three to four percent.

DR. L. KAPLAN: How do you handle small and large prolapses?

DR. CORCORAN: I have not had too much experience with prolapses. The small prolapse was clipped off and the wound resu-

tured. There have been no cases of epithelial downgrowth. However, because of the increased number of sutures, the patients do have red eyes.

DR. FREEMAN: Why did you jump from two to 10-percent novocaine? Why that particular percent? I feel that many corneoscleral sutures hit the base of the iris, as has been shown in animals. Also, the general surgeon does not tie sutures too tight. The removal of sutures is not too difficult. I believe that the more perpendicular to the surface is the incision, the fewer sutures will be necessary. A slanted incision requires more sutures. I also feel that some of the suture material must remain in the wound, and this may explain the red eyes.

DR. CORCORAN: As to the 10-percent novocaine, I used it because Dr. Scheie has used it for several years without complication. Ten-percent novocaine plus massage is terrific if you like to work on a soft eye. Adrenalin is used because the anesthesia wears off too soon without it, especially with hyaluronidase. I am positive the sutures do not go below one-half the corneal thickness and do not go to the base of the iris. The sutures are purposely designed to slough out. I agree that the number of sutures depends on the type of section.

Dr. Wies: I think there is some confusion with regard to the term, "soft eye." After the eyeball is open, the pressure is the same —one atmosphere—regardless of the preoperative preparation. In regard to removal of sutures, it takes time and patience. If you wait at least 10 minutes after initial instillation of pontocaine and cocaine, there will be no trouble.

DR. CORCORAN: You are right about the soft eye. I try to get an eye soft before it is opened. I am really talking about a reduced vitreous volume produced by massage, which milks out retrovitreal or intravitreal fluid, and, also, I am aiming for better anesthesia. I want to get a vitreous that falls back when the eye is opened. I still believe suture removal is generally considered difficult and somewhat risky.

DR. WONG: I noted you released the erisophake and then applied capsule forceps during the process of extracting the lens. Is this necessary?

DR. CORCORAN: No. I probably do not have a good enough erisophake.

DR. MILTON BERLINER, New York, discussed two main topics, "Cyclodiathermy for glaucoma," and "Vitreous pathology."

CYCLODIATHERMY FOR GLAUCOMA

DR. BERLINER compared cyclodiathermy for glaucoma in a first series of 69 cases with his second series of 100 consecutive cases. He likened cyclodiathermy to surgical Diamox therapy. In the first series, his failures, in follow-up of one and one-half to two years, were about four percent contrasted to about 12 percent in his second series. Cyclodiathermy was performed in penetrating fashion with a 1.5-mm. needle about 5.5 mm. from the limbus in all four quadrants.

He felt that, with the exception of glaucoma with rubeosis, if there was no lowering of pressure after two operations, another operation was not indicated. In rubeosis, since the prognosis was so bad, even a third operation was indicated. Phthisis bulbi appeared in a few eyes.

Dr. Berliner believed that 5.0 to 5.5 mm. behind the limbus was the position of choice because the type of bipolar ganglion cells located at this area seemed instrumental in lowering the tension. He also noted that, if there was no rise of pressure about 15 minutes after the cyclodiathermy, the prognosis was poor. The danger in going too far back is that it may cause retinal detachment, which has been reported but which he did not note in his series. Going too far back may cause a vitreous reaction with shrinkage of the vitreous. He never noticed the complication of a soft eye with 16 punctures.

The problem of how much current to use was also discussed. At present there is no way of exactly measuring the amount of current used in this method and the effect of a

given machine setting varies from patient to patient. Dr. Berliner endeavors to get enough current so that the needle goes in easily. If sizzling occurs, too much current is being used. He also presses the spot to be treated with a muscle hook before applying the diathermy needle in order to approximate the conjunctiva to the sclera as closely as possible. He noted that the eye may stay red after the operation for a period of two months.

Dr. Berliner's talk was followed by a short movie which demonstrated lucidly the essentials of the procedure.

Discussion. Dr. Blake: I was enthusiastic at first about cyclodiathermy, then not so much later on. At first I tried punctures at four mm. from the limbus, then at eight mm., but I had two retinal detachments when using the latter distance. I believe four mm. is the better distance for treatment. In regard to anesthesia, I wait at least 10 minutes after retrobulbar injection and, in addition, apply cocaine locally at the sites to be treated. It is a simple procedure. I have done it in my office and I believe it has a place in therapy. I generally would do two upper-quadrants at one time, repeating the procedure below at a later time if necessary.

Dr. Fasanella: Dr. Chandler thought the operations that worked well were due to permanent drainage at the puncture sites and I believe he said that he had three detachments.

Dr. Wong: Does cyclodiathermy lessen nutrition to the lens?

Dr. Berliner: Cases two years postoperatively showed no lens changes in contrast to frequent lens changes after decompression operations.

Dr. Kaplan: Have you used it in congenital glaucoma?

Dr. Berliner: Only in a case where three previous operations were done; the result was poor.

Vitreous pathology

Dr. Berliner discussed the difficulty of viewing the deep vitreous with different methods available. In all methods, the pupil must be well dilated. A contact lens is clumsy. The image is slightly larger and clearer but you cannot see as well peripherally with it. The Hruby lens allows deeper penetration of the vitreous by overcoming the dioptric power of the cornea.

The vitreous was described as not a pure gel but as being a complex structure with branching framework including a hyaluronic-acid gel in the meshes. In the so-called fluid vitreous the fibrillas contract and break up, extruding the fluid. This is not true liquefaction.

Two normal types of vitreous were described: the lamellar and the fibrillar.

Changes in the vitreous are nonspecific. Endogenous changes begin at about 40 years of age, earlier in myopes, starting in the periphery. Dr. Berliner discussed the so-called detachment of the posterior face of the vitreous. It has not been determined whether it is really the hyaloid or the back surface of a contracted portion of fibrillar vitreous. The condition is said to be very common, almost 100 percent in myopes and almost 90 percent in people over 55 years of age.

Clinically there are flickering of lights, phosphene, and a vitreous opacity. A large opacity has a structure and is usually attached to the posterior surface of the vitreous. There may be holes in the posterior surface and occasionally some vitreous structure herniates backward through the holes. Vitreous detachment does not seem to cause much harm. Dr. Berliner felt it usually detaches completely and believed that fortunate and less likely to result in retinal detachment than if it remained attached to a weak spot in the retina. In very high myopia detachments often do not develop for this reason.

Rupture of the anterior hyaloid may occur after cataract extraction, up to three years postoperatively. With vitreous in the anterior chamber the patient develops some redness with or without pain and blurring of vision. Statistically this occurs in 17 to 20

percent of all intracapsular, round-pupil extractions, and in seven to nine percent of all iridectomy extractions. Frequently nothing else happens but, if a lot of vitreous herniates into the chamber, such complications as retinal detachments, glaucoma, distorted pupil, and contraction bands may develop. The cause of spontaneous anterior hyaloid rupture is not known.

Dystrophy of the cornea may result from adhesions to the posterior surface and is usually progressive. If the endothelium is intact, vitreous will not adhere. Air injection may help. In cases of corneal dystrophy preoperatively, Paufique has done endothelial scarring followed by corneal transplantation and then the cataract extraction.

Discussion. Dr. Fasanella: Dr. Paton has also advocated early corneal transplantation for guttate keratitis.

William Glass,
Recording Secretary.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

November 1, 1954

Dr. Frederick H. Theodore, *President*

Newer concepts in treating external eye disease

Dr. Frederick H. Theodore pointed out that it is becoming increasingly important for the physician to assume a more critical approach when appraising the many new drugs that are now available for ocular therapy. Because most of these drugs are indeed of great value, there is a natural tendency to accept *all* of the newer medicaments on the basis of what is claimed for them by the manufacturer.

Until recently, antiseptics were rated in terms of phenol coefficiency. This method is no longer considered applicable for most antiseptics. It is now recognized that any laboratory testing of antiseptics must be followed by practical in vivo tests, toxicity determinations, and by clinical tests under the practical conditions for which such preparations are recommended. The testing of antiseptics is obviously not a simple matter, and reliance on any one in vitro test is exceedingly dangerous.

Important factors making the in vivo action of an antiseptic an entirely different matter from the in vitro action are: (1) absorption; (2) tissue affinities; (3) spreading factors; (4) concentration; (5) stability; (6) rate of drug metabolism; (7) pH of tissues; (8) protein binding of drugs; (9) effect of body fluids; (10) presence of natural inhibitors; and (11) the resistance and metabolism of the micro-organism itself. All these factors may completely vitiate in vitro findings, so that clinical observation is often the last court of appeal.

Mercury is a good example of the above. In vitro, its compounds are highly antiseptic, but all mercurial products are inactivated in the presence of SH radicals, organic matter, and serum.

The quaternary ammonium compounds, such as benzalkonium chloride, better known as Zephiran, have capricious actions both in vitro and in vivo. Below are noted some of the drawbacks of benzalkonium:

1. Diminished effect in the acid pH range.
2. Relative ineffectiveness against gram-negative organisms, such as Ps. aeruginosa (B. pyocyaneus).
3. Inactivation by: (a) anionic wetting agents such as soaps and phisoderm; (b) calcium and magnesium ions (hard water); (c) ferrous and ferric ions (such as tap water); (d) phospholipids; (e) body fluids; (f) rubber; and, (g) linoleum, including vinyl plastic.

Benzalkonium is not advocated for sterilizing instruments, nor for the preoperative preparation of eye patients.

The best results in the sterilizing of the skin are obtained with iodine and alcohol. Alcohol deservedly enjoys a high place among the antiseptics. It is very effective against Ps. aeruginosa. The alcohol content

of tinctures of metaphen, merthiolate, and Zephiran is the chief reason for their efficacy.

It is now required by Federal regulation that all commercially prepared ophthalmic solutions must be made sterile and contain suitable preservatives. Recent investigations have confirmed that Chlorobutanol is usually the best preservative for this purpose. Since there are no regulations concerning the preparation of eye solution by hospital pharmacies or by retail drug stores, it would appear advisable for the ophthalmologist to routinely prescribe 0.5-percent solution of Chlorobutanol as a vehicle for all individually prepared ophthalmic prescriptions. Not only does Chlorobutanol appear effective in preserving solutions originally prepared sterilely, but it has also been shown to be useful in sterilizing solutions contaminated experimentally.

The importance of sterilizing tonometers after use, to prevent the transmitting of virus diseases such as epidemic keratoconjunctivitis, cannot be overemphasized. The only sure method appears to be heat sterilization. The use of dry heat, such as passing the foot-plate of the tonometer through an alcohol flame appears effective and does not seem to injure the tonometer. Devices permitting more accurate control of the heat necessary for sterilization are being tested. Antiseptics are not reliable for this purpose and appear to injure the tonometer.

One should emphasize the untoward effects that may occur due to antibiotic therapy. These include: (1) allergic (contact dermatitis, drug fever, serum sickness, and anaphylaxis); (2) toxic and irritative effects (renal, hepatic, hematologic, neurologic); (3) biologic alterations (changes in the microbial flora sometimes resulting in the conversion of a minor infection into a serious or even fatal disease).

The local use of antibiotics is indicated in corneal and intraocular infections, or in unusually serious conjunctival or lid infections. In regard to corneal ulcers, the taking of the culture itself may often be good treatment, because the removal of necrotic material eliminates the presence of substances that may inactivate the antibiotics used and also permit better penetration of the medicament. Combinations of antibiotics, including the use of drugs which on sensitivity tests are not outstanding, often may be better than relying only on one apparently efficacious drug. This is so because different antibiotics may affect varying enzyme systems in the bacteria, and, in this manner, more readily eradicate the infection.

The sulfonamides are very useful drugs in the treatment of external ocular infections. Their main drawbacks, however, are the tendency to result in allergic reactions and bacterial resistance. Fatty acids, such as sodium propionate, on the other hand, are much less prone to sensitize, and thus are of definite value in most infections and for long term usage. Ten-percent solutions of this drug at a pH of 6.0 are advocated. The drug is particularly effective against gram-negative organisms. The basis of its activity in inhibiting the growth of Streptococcus faecalis is believed to be the inhibition of sodium acetate formation by this bacteria.

Useful techniques in ophthalmology

Colonel John H. King, Jr., mentioned certain phases of ophthalmology which he had observed during a two and one-half month trip to Europe, during which he visited U. S. Army hospitals and certain civilian medical centers. He elaborated upon various techniques and research noted in Europe along with current practices in the United States.

The vision testing devices for malingering as used by Prof. Weve and Prof. Goldmann were described. A new instrument to determine visual acuity in young children developed by Schwarting at Walter Reed was mentioned. A review of orthoptics in Europe and a description of Bietti's use of oxygen as a supplement to orthoptic training were given. Ocular diseases caused by leptospiro-

sis, toxoplasmosis, and trachoma were discussed, and the sterility of solutions was commented upon.

Colonel King described in detail the value of the Amsler grid technique in determining early functional disturbances of the macula and showed examples of its use. He explained the causes of micropsia and macropsia and felt that early treatment might prevent a well-established organic condition which will not respond to therapy. A brief explanation of the Haidinger brush phenomenon and its value in detecting early macular disease was given.

An interesting discussion of ocular surgery in Europe as compared to the United States covered numerous techniques. Bietti's small plastic lens which is placed in the anterior chamber six months following the removal of traumatic cataract was demonstrated in detail and compared to Ridley's lens in the posterior chamber. The Arruga implant following enucleation was described, and a new buried implant used by the military services was shown.

Certain phases of ocular research being performed in Europe and in the United States were discussed. Studies covering hyperoxia, anoxia, tonometry, and electroretinography were noted as new developments. The electroretinogram findings in American prisoners of war in Korea with nutritional amblyopia prove for the first time that at least one site of the pathology is in the retina.

Colonel King concluded with comments concerning ophthalmologic teaching in Europe and elaborated upon the excellent instruction which is again available at the two eye clinics at the University of Vienna.

Colonel King also showed a sound movie which depicted preliminary experiments with the ocular metamagnet, designed to attract nonmagnetic metallic intraocular foreign particles. This electronic magnet uses a 25-kilowatt amplifier with 8,000 cycles. It attracts two-mm. particles of copper, aluminum, and brass eight to 10 mm. distance with good pull. Experiments with these particles in cat eyes were shown. The magnet has not yet been applied to clinical ophthalmology, and there are still many problems to be solved in its power and design.

Jesse M. Levitt,
Recording Secretary.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

Section on Ophthalmology

October 21, 1954

Dr. Edmund B. Spaeth, M.D., *Chairman*

Hyaluronic acid and hyaluronidase in aqueous humor and chamber angle

Dr. Ernst Báràny, Uppsala, Sweden, said that the resistance to flow through the chamber angle of excised animal eyes is reduced to about half by small amounts of testicular or bacterial hyaluronidase. This indicates the presence of mucopolysaccharides in the outflow barrier. A search was made for hyaluronidase in the aqueous humor, which might have been an important controlling factor for the outflow resistance. No evidence for the existence of the enzyme in the aqueous was found. The mucolytic properties of the aqueous in vitro are explained by its ascorbic acid content.

Lowering the intraocular pressure by unilateral carotid ligation in rabbits leads to an increase in the resistance of the angle. Increasing the intraocular pressure by venous obstruction decreases the resistance of the angle. The resistance of normal rabbit eyes is unaffected by prolonged treatment with progesteron ointment but lowered by cortisone and cortisol.

William E. Krewson, 3rd,
Clerk.

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SIXTIETH ACADEMY MEETING

The 60th annual meeting of the American Academy of Ophthalmology and Otolaryngology, under the roborant presidency of Algernon B. Reese of New York, was held at our favorite place, the Palmer House, Chicago, October 9th to 14th. The attendance was record breaking, the weather gorgeous, the atmosphere of the meeting reasonably benign, and the scientific program with its ancillaries most noteworthy.

At the opening (joint) session, President Reese most graciously introduced the guest-of-honor, Alan C. Woods of Baltimore, and the honor guest, Sir Norman Gregg of Sydney, Australia, and gave a short and laudatory biographic sketch of each. The address by the president was "Pathology." Dr. Reese

pointed out that modern pathology is not the decadent science it formerly was considered to be. On the contrary, due to new scientific tools and exciting techniques this discipline is indeed very much alive. The marked improvement of "methodology," such as the electron microscope, new lighting, dynamic cytology or phase contrast, microfluorescence both from the cells themselves and from the use of fluorescent lighting—for example, identity of tumor cells, the identification of allergic diseases—cytochemistry, cytophotometry and tissue culture, especially in the last eight years, have explosively opened for us thrilling new avenues of approach to the solution of medical problems, particularly in ophthalmology. Dr. Reese went on, in tribute, to say that Verhoeff was the father of American ophthalmic pathology; that he now has, in the Ophthalmic Pathology Club of 35 members, a "flourishing family speaking the patois." As a self-trained and sufficient pathologist, Verhoeff is said (Parsons) to have "left a trail of blood" among European ophthalmologists after his tour of England and the Continent in the early part of this century. Dr. Reese then pointed out the value to the clinician of a good pathologic report. He entered a plea for a closer contact between clinician and pathologist, and urged the latter to familiarize himself with the new techniques and utilize them for the advancement of our knowledge. The address was most scholarly, informative, and witty.

Dr. Woods spoke on the "Role of the Academy members in the changing pattern of medicine." This thoughtful and courageous address will appear in full in the *Transactions*, but the main theme was that the Academy should take a firm stand on the training and ethics of ophthalmologists who are swirled about in the changing currents of the economy to which we are now exposed.

Following the presentation of a special award to Franz Altmann, M.D., for his part in the production of the Academy film "The embryology of the ear" and honor awards to nine members of the Academy, a symposium on "The uses and abuses of the corticosteroids in ophthalmology and otolaryngology" was held. John McLean of New York spoke on the "Ophthalmologic aspects," Aubrey G. Rawlins of San Francisco on the "Otolaryngologic aspects," and Rachmiel Levine of Chicago most delightfully on "General considerations," urging caution and informed conservatism in the use of these substances.

The XII Jackson Memorial Lecture was given by Frederick C. Cordes of San Francisco. His subject was "Failure in congenital cataract surgery: A study of 56 enucleated eyes." The lecture was admirably presented and beautifully illustrated. Dr. Cordes had collected his material from many sources, including the Armed Forces Institute of Pathology, and skillfully analyzed it so that conclusions, valuable in surgery, could be drawn. His published paper will bear careful study.

On each of the ensuing four mornings, the scientific session began with a clinicopathologic case report. This is an attractive and informative feature, effectively pointing up the importance to the clinician of a good pathologic report.

Then followed scientific papers with or without formal discussions and usually alternating with an excellent film of ophthalmic interest. Three of the most outstanding of these were "Clinical applications of electroretinography," by Jerry H. Jacobsen; "The effects of oxygen on retinal vessels," by Norman Ashton; and "Oxygen in retrolental fibroplasia: Ophthalmologic aspects," by Arnall Patz.

This year's featured symposium was on "Diseases of the optic nerve." The subjects covered were the anatomy, physiology, symptoms, and signs; pathology; basic concepts; congenital anomalies; classification; spread of inflammation from adjacent structures; systemic infection producing optic nerve diseases; lues; multiple sclerosis and allied diseases, pathology of these affections; hereditary affections, circulatory disorders, trauma, noninfectious diseases, nutritional amblyopia, toxic amblyopia, tumors and op-

tic neuritis of unknown etiology. Those taking part in the panel were Frank D. Carroll, John W. Henderson of Ann Arbor, Lorenz E. Zimmerman, Frank B. Walsh, and C. Wilbur Rucker. The material was austerely arranged and delivered by each participant with well-rehearsed precision. These symposia now have become one of the most valuable and popular features of the meetings. The large ballroom was entirely filled with seated and standing members who gave rapt attention to the entire presentation.

Ocular anesthesia was the subject of four papers, and the newer steroids—Prednisone and Prednisolone—were discussed in three papers.

Sir Norman Gregg of Sydney, Australia, gave a delightful address on the "Relationship of infections in the early months of pregnancy to congenital anomalies." He cited his early work associating rubella with congenital cataract and elaborated on many newer studies pertinent to his subject.

Prof. Dr. A. Pillat of the I. Eye Clinic, Allgemeines Krankenhaus, Vienna, and successor to Professor Meller, discoursed on "The aging of the retina" in classic form. During the short intermission that followed his talk, Professor Pillat was quickly surrounded by a horde of his former pupils, some of whom conversed in fluent German with their master, giving an air of "reunion in Vienna," without libation or music.

At various times during the week, various organizations, or wheels within the wheel, held their special scientific sessions. These were the American Orthoptic Council, meeting jointly with the American Association of Orthoptic Technicians, holding a symposium on "Amblyopia"; Industrial Ophthalmology, whose symposium was on "Foreign bodies"; Committee on Plastic and Reconstructive Surgery, the teachers section where Alan C. Woods gave a thought- and discussion-provoking paper on "Undergraduate instruction in ophthalmology," and finally a special meeting of the American Society of Ophthalmologic and Otolaryngologic Allergy, where the ophthalmic group held a good symposium on the "Allergic and collagen diseases of the eye."

An evening was devoted to the showing of two special films, the "Surgical treatment of lid tumors" by Algernon B. Reese, and the outstanding feature of interest to ear, nose, and throat colleagues "The embryology of the ear," sponsored by the Academy, produced by Sturgis-Grant Productions, Inc., and directed by Franz Altmann, M.D.

As if all this were not enough an excellent daily program of ophthalmic and otolaryngologic surgery was televised in color from the Illinois Eye and Ear Infirmary, Chicago, by Smith, Kline, and French Laboratories under the auspices of the Committee on Television consisting of Walter H. Theobald, William F. Hughes, Jr., Frederick J. Pollock, and Maria Ikenberg, F.B.P.A., technical assistant.

Each afternoon, as usual, was devoted to the Section on Instruction in Ophthalmology; there were 122 individual courses, and 53 continuous courses given by a faculty of 219 instructors. The total number of hours of instruction was 403. All ophthalmic subjects were covered and many of the courses were sold out. In addition there was a well-attended free lecture on "The practical application of electroretinography in diagnosis and treatment" by Dr. Harold E. Henkes, Rotterdam, Netherlands.

Fifteen of the 29 scientific exhibits presented pertained to ophthalmology. Of these, the beautiful exhibit, "Pathology of the vitreous in retinal detachment" by Chih Chiang Teng and Helen H. Chi of the Eye-Bank for Sight Restoration, Inc., was awarded first prize. The second prize was won by Hermann M. Burian, Alson E. Braley, and Lee Allen from the Department of Ophthalmology, College of Medicine, State University of Iowa for their exhibit on "A new concept of the development of the angle of the anterior chamber of the human eye," and the third prize was given to Martens, Sayre, Craig, and Kernohan of the Mayo

Clinic and Mayo Foundation, Rochester, Minnesota, for their fine teaching exhibit on "Tumors of the region of the optic chiasm: mechanism of the production of visual loss."

There were very many commercial or technical exhibits as usual, and the latest in books, instruments, and equipment was eagerly investigated mainly with an eye to purchase.

The social side of the meeting was well represented by the president's reception and the banquet. The latter, instead of being the usual starchy and sturdy affair it had been in the past was a delightful evening of no speeches, a captivating surprise, and a good floor show followed by dancing into the wee hours. It was an overwhelming success. The usual alumni dinners were held in various parts of the town, and the faculty luncheon had an entertaining gag, arranged for by our peripatetic president, that enlivened this occasion.

At the business meeting, Sir Norman Gregg, Prof. Arnold Pillat, Prof. Adolph Franceschetti, Prof. H. J. M. Weve, Dr. Henry Imus, Prof. Raúl Arganaraz, and Dr. Edward Hartmann were elected Honorary Fellows.

The officers for 1956 are Dr. A. C. Furstenberg of Ann Arbor, Michigan, president; Dr. Erling W. Hansen of Minneapolis, president-elect; Dr. M. Hayward Post of St. Louis, first vice-president; Dr. Henry L. Williams of Rochester, Minnesota, second vice-president and Dr. Walter S. Atkinson of Watertown, New York, third vice-president. The 1956 meeting will be held October 14th to 19th, at the Palmer House, Chicago.

So closes the 60th annual meeting of our great Academy. It was an outstanding one, surrounded by an aura of courtesy, precision, and great good humor, and reflected in great measure the scientific character and good-natured fellowship of our able president, Dr. Reese.

Derrick Vail.

THE TRAINING OF AN OPHTHALMOLOGIST

The subject of the recent May Memorial Lecture, delivered at the New York Academy of Medicine, was "The training of an ophthalmologist." In this lecture it was emphasized that the first important step in the successful training of an ophthalmologist was the selection of proper material to train, for it is axiomatic that no man can build a good house out of poor timber. Since all trainees intend to take the examinations for certification in their specialty at the completion of their training, it is obvious that in the selection of the personnel to be trained the prerequisites of the various specialty boards must be considered.

The 1955 brochure of the American Board of Ophthalmology states various prerequisites for examination. The fourth of these prerequisites is as follows: "Completion of an internship of not less than one year in a hospital approved by the same Council" (that is, the Council on Medical Education and Hospitals of the A. M. A.). Prior to July, 1955, the Council on Medical Education and Hospitals approved specifically rotating internships, and straight internships in medicine, surgery, pediatrics, and pathology. It also gave to certain teaching hospitals a blanket approval. When these hospitals offered internships in various specialties, such internships came under this blanket approval, and medical students applying for such specialty internships were admitted to the "Matching Plan" and duly assigned to these services. This fully met the requirements of the American Board of Ophthalmology, although such trainees were required to have an additional year of experience in practice before they were eligible for examination.

The value of the required preliminary internship for some time has been a question of debate and considerable difference of opinion. On the one hand, no intelligent medical educator can possibly deny that a

broad graduate training in medicine, surgery, and pathology widens the horizon of the future ophthalmologist and makes him a better man. In theory this requirement was excellent. In practice, there was considerable reason to believe that this prerequisite did not work for the advancement of ophthalmology, but to its detriment. The reasons for this belief were as follows.

Many first class medical students become interested in ophthalmology during their undergraduate medical years and before graduation decide to make it their life work. Confronted with the requirement of a year's preliminary approved internship, these students naturally sought the best obtainable internships, usually in the teaching hospitals and frequently in those connected with the institution from which they were graduated. Being top-flight students they obtained these choice internships under distinguished chiefs. But these distinguished chiefs, keenly on the lookout for the best material, were loath to surrender these excellent men to ophthalmology when the end of the intern year was reached. They therefore offered them appointments in the higher echelons of their services. The intended ophthalmologist, in the most formative years of his life, interested in his work, influenced by the famous physician under whom he was serving, with an offer before him which almost assured his future, rarely if ever refused such offered appointment. He was thus weaned away from his first love and lost to ophthalmology. The cream of the crop was culled in this preliminary intern year. The castoffs were left for the specialties!

The average good medical student who did not obtain a medical or surgical appointment in a teaching hospital, usually took a rotating internship in one of the nonteaching hospitals. The value of this rotating service to the future ophthalmologist was seriously questioned. In the successive quarters of medicine, surgery, obstetrics, and the specialties, the intern was under the guidance of chiefs, who, while undoubtedly able internists and surgeons, were also usually woefully ignorant of the special medical and surgical problems which would later confront the ophthalmologist. The future specialist therefore did not receive the training best suited to his needs. Too often the rotating internship was a wasted year; often little more than a repetition of the fourth year of the medical school and under the guidance of chiefs-of-service who were under no obligation to teach.

The directors of the ophthalmology services in both the general teaching hospitals and the special ophthalmic hospitals therefore found themselves plagued by the continued seduction of their brightest prospects during the required preliminary intern year, and distressed by the inadequately trained material arriving from the rotating services. To obtain better material to train, the natural inclination was to turn to the newly graduating classes. Here they encountered the difficulty of the American Board's requirement of a year's approved preliminary internship. But this difficulty was not insurmountable for the teaching hospitals which had been approved by the Council on Medical Education and Hospitals of the American Medical Association. The first year's service in ophthalmology in these approved hospitals fully met the requirements of the American Board of Ophthalmology, and likewise filled the requirements of those state licensing boards which required an approved internship. Under this arrangement, the ophthalmology service of a teaching hospital could compete with other services in the quest for the best material. This scheme worked, and worked well, and it can be truthfully said that in the years this policy was in force many of the best men developed in ophthalmology were the top-flight medical students who began their training in ophthalmology directly after graduation without a preliminary internship elsewhere. However, in 1953, this well-working scheme was suddenly interrupted.

On July 30, 1953, without previous warn-

ing of any kind, and without consultation with ophthalmologists or with the American Board of Ophthalmology, the Council on Medical Education and Hospitals suddenly withdrew their previous indirect approval of these straight specialty internships offered by the teaching hospitals, and now limited their approval specifically to straight internships in the medical, surgical, and pediatric services, and to rotating internships. Later, the council gave approval to straight internships in pathology and obstetrics. The first year's training in the other specialties was now classified by the council as "assistant residencies." The reason for this sudden action is not clear. It might be assumed that this ruling was made to force graduating medical students into general rotating internships in the nonteaching hospitals which were hard pushed to obtain sufficient interns to meet their basic needs. The secretary of the council, however, states this is not so and further states that this reclassification of the first year of specialty training is in no way a reflection on the excellence of the service, but is merely a question of semantics. Whatever may have been the reason underlying this action of the council, the effect of this ruling was instantaneous. Almost without exception, men who were to graduate in 1954 and who had previously planned to embark directly on their training in ophthalmology, either did not apply or withdrew their applications. As far as can be ascertained, there was only one such application from a 1954 graduate, and none have been received from the men who are to graduate in 1955.

The seriousness of this action of the Council on Medical Education and Hospitals is evident. It has almost completely shut off the flow of the best material into ophthalmology. True, some first class men who originally planned to enter ophthalmology, survive the enticements offered by the services in which they take their intern years and persist in their original intention. But these are not many. In general, it is true that the majority of men applying for training in ophthalmology are either the cast-offs of other services or veterans returning from military service. Unfortunately, there is not a great deal in the military service of young medical officers to stimulate an undue appetite for ophthalmology. It is to be sincerely hoped that the Council on Medical Education and Hospitals will reconsider its former action and restore to the "approved" status the first year of ophthalmology in those hospitals which can and do offer all the necessary ancillary facilities for graduate training.

Alan C. Woods.

OBITUARY

FRED T. TOOKE
(1873-1955)

Dr. Fred T. Tooke of Montreal passed away on July 20th, at the age of 82 years. He had been in failing health for several years. His markedly sunny and happy nature coupled with his great natural abilities made

FRED T. TOOKE, M.D.

him many and lasting friendships wherever he went. He was one of Canada's leading ophthalmologists, and as such travelled widely. His many friends in Europe and America will be sorry to hear of his passing.

Frederick Thomas Tooke was born in Montreal in 1873, where he had his primary education at the school of the Church of St. John the Evangelist and at the Montreal High School. He then entered McGill University which granted him a B.A. degree in 1895.

In these days of great discussion and soul searching relative to the best method of teaching an ophthalmologist, it is interesting to see how one of our elders went about it. Dr. Tooke was graduated in medicine from McGill in 1899. Following this he served for three years on the house staff of the Royal Victoria Hospital, Montreal—one year each in medicine, ophthalmology, and as admitting officer. Dr. Frank Buller was at that time professor of ophthalmology at McGill. On his advice, Dr. Tooke made a grand tour in Europe, as was the custom among those who aspired to high things in those days. This tour covered three years during which he served as clinical assistant for a year each under Prof. Axenfeld at Freiburg, Prof. Morax at Paris, and under Sir William Lister and Mr. Marcus Gunn at Moorfield's, London. He also studied for a short period in Vienna.

In 1905, he returned to Montreal and opened his practice in ophthalmology in which he was most actively engaged for the next 45 years. At this time he joined the ophthalmic staffs of McGill University and the Royal Victoria Hospital. He steadily rose in the ranks of both institutions becoming ophthalmologist-in-chief at the Royal Victoria Hospital from 1935-1940, and professor of ophthalmology at McGill University from 1937-39. He retired from his practice in 1950.

Throughout his long and busy professional life, Dr. Tooke made many contributions to ophthalmic knowledge. These for the most part were of a clinical or pathologic nature. He will be remembered for his introduction of a cornea-splitting knife for use in the Elliot trephining operation. He was an active member of the Montreal, the Canadian, and the American Ophthalmological Societies. He had been past president of all three and a charter member of the first two. He also was active in the Canadian Medical Association and the American Academy of Ophthalmology and Otolaryngology. He kept up his many European friendships through his membership in the Ophthalmological Society of the United Kingdom and the Société d'Ophtalmologie Français.

In 1907, he married Katherine Morecroft Tomlinson. This ideal union was not only a source of great happiness but also of great assistance, as Mrs. Tooke was the doctor's constant companion and confidente until her death in 1952. There were six daughters of this union all of whom survive.

John V. V. Nicholls.

CORRESPONDENCE

Visual impairment from NP 207

Editor
American Journal of Ophthalmology:

At the City County Hospital here we have encountered some very startling and serious results from the use of a new drug NP 207 issued by the Sandoz Company and used experimentally by the neuropsychiatric service in an effort to replace Thorazine.

All patients receiving over 30,000 mg. have had serious visual impairment, and two who had between 20,000 and 30,000 mg. The symptoms are as follows:

Within three to four weeks after the drug is started, the vision becomes blurred and rapidly drops to 20/200 or hand movements. If the drug is discontinued early there is some recovery, but not much. The earliest recognized sign is an increase in the number of retinal reflexes, probably due to slight edema. The retinal veins and arteries then become somewhat dilated and the papilla is

quite pink. Field changes consist of severe narrowing or annular scotoma.

A little later small pigment clumps appear in the midperiphery and spread toward the ora and toward the disc, involving the macula last. The disc has remained pink, although the oldest case we have observed is nine weeks. The arteries have narrowed somewhat but the veins are still moderately engorged. The pigment in the oldest cases has now formed sheets in the choroid and in some places the sclera is exposed. Thirty-three patients received the drug and 22 had evidence of retinal disturbance.

After the use of the drug was started here, a report came from Switzerland that some cases there had shown visual disturbance, and its use was soon discontinued. I believe the people who were supplied with the drug have all been warned.

I suppose it is too late to serve as a warning. Dr. Mary Fletcher, senior resident in ophthalmology at Jefferson Davis Hospital, has discovered and followed these cases carefully.

(Signed) Everett L. Goar,
Houston, Texas.

Adjustment to aphakia

Editor
American Journal of Ophthalmology:

A friend has just brought to my attention a reprint of "The adjustment to aphakia" which appeared in the January, 1952, issue of The Journal. According to the footnote it was written by a physician who had successfully had bilateral cataracts removed.

Although I write from the lay point of view, I hope The Journal will print this letter, because such an article as the unsigned one referred to is lulling ophthalmologists into a defeatist attitude toward visual aid for aphakic patients.

I, too, am a bilateral aphakic. My first cataract was removed in March, 1952, at which time vision was discernibly impaired in my other eye. Some months later an obstructing membrane was needled in my aphakic eye.

The writer of The Journal article speaks of spherical aberrations; because in my case the aperture derived from needling did not heal smoothly, but with twisted edges turned in contrary directions, these spherical aberrations became so exaggerated and so manifold that the wearing of the spectacle lens over that eye caused acute nausea. Vision in my unoperated eye had deteriorated so it hardly sufficed for close work but, with the lens over that eye occluded, I could see for close work through the aphakia lens.

I could not get around out of doors with it, however. It was not a question of things being bowed out; they were also bowed in. The sidewalk was often on three levels. I was to learn months later that there were three points of light reflex in that eye.

If I had been a patient of the man who wrote your article I would have been judged one of the neurotics he has included in his third group. Fortunately the ophthalmologist under whose care I was did not set aside my difficulties by such a sweeping generalization. He suggested my having a contact lens made for the aphakic eye. Because, learned as my ophthalmologist is in the surgery of the eye, he is a neophyte in the evaluation of contact lenses, and even more so in his knowledge of the essential importance of who makes the lens, the history of my efforts to get the right contact lens is a long one. I have discovered my ophthalmologist is not alone in his lack of contact lens knowledge among ophthalmologists.

At long last, through the scientific zeal of a contact-lens specialist of high integrity, I got a lens that gave me better than 20/20 vision in my aphakic eye.

Speaking from my own experience, I can contradict some points in The Journal article. In the next to the last paragraph on page one, the statement is made: "Useful binocular vision is impossible until the second eye is operated on." That is not true. For at least a year after I got my correct contact lens for the aphakic eye I had binocular

vision—that is until the sight of my unoperated eye grew so dim it was not seeing. The contact lens reduced images to normal size, and because the lens moved with my eye, I had depth of focus and a wide field of vision. Later when my unoperated eye lost its usefulness I depended upon the aphakic eye wearing the contact lens.

In the second paragraph in the second column of the next page, there is reference to the need for moving the head to bring objects into focus. The contact lens, which so nearly approximates the natural lens, and has its motion with the eye itself, obviates the necessity for moving the head to focus.

Ophthalmologists have so come to accept the idea of channeled vision for the aphakic they have failed in too many cases to give them the now available freedom from this visual stricture, which is offered by the contact lens.

Referring to the first and second paragraphs on the third page, the answer is the same. I cannot be emphatic enough in saying the aphakic need not be dependent upon the mercy of the innocent stranger who might collide with him on the stairs, or the motorist who might run him down on the street. True, he is thus handicapped if he wears the limiting spectacles, but why should he, unless prevented by some unfortunate systemic contraindication, when contact lenses will give him motility of vision?

In the last paragraph of the article the statement is made: "The problem concerns the elderly individual without great visual requirements whose vision is reduced only to the 20/70 or 20/100 level." What about us who had 20/20 vision before the onset of cataract? What of those who are not so old? I hope I have some productive years ahead of me. I love the beauty of a rose, the delicacy of fine lace, the carving of a piece of jade, all the loveliness surrounding me just as much as I did when I was a young girl; maybe even more, because the cataract-induced lack of vision while waiting for surgery showed me what loss of sight means.

Seven months ago I had the cataract removed from my other eye; this time quite successfully. I still have the aberrations in my left cornea, and my aphakia spectacles still cause nausea because of them. The contact-lens specialist told me I would have to wait at least six months after surgery before he would make a lens for my other eye, because there might be postoperative edema of the cornea. Now he is ready to make the lens for me, and I feel that I am standing on the threshold of something like recaptured normalcy of vision.

No, Dr. Unknown Aphakic, you have no right to damn other aphakics to your own unnecessary visual limitations. To all ophthalmologists who read THE JOURNAL I address this plea for the best possible vision for aphakics. It isn't enough to just "get by" visually when something more than that is available. It is high time that ophthalmologists inform themselves of the great potential worth of contact lenses in helping organic eye troubles, including aphakia, and that they be sure the lenses are made and fitted by technicians who know what they are doing, have scientific integrity, and supply contact lenses only when prescribed by ophthalmologists.

Action is overdue by the society of ophthalmologists in outlawing the indiscriminate advertising, prescribing, and fitting of contact lenses. These small plastic miracles have as great potentiality for harm as they have for good. They become a hazard to the public which falls into the greedy hands of those optometrists who are ready to insert them in any proffered eyes, whether necessary or not, and often where they can do lasting injury.

Having brought into being a law which would make it a criminal offense to supply contact lenses without a qualified ophthalmologist's prescription, I urge you to use them for the aphakic, for whom they mean rebirth visually.

(Signed) Annette M. Snapper,
Milwaukee, Wisconsin.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Allen, L., Burian, H. M., and Braley, A. E. **A new concept of the development of the anterior chamber angle.** A.M.A. Arch. Ophth. **53**:783-798, June, 1955.

A new concept of the formation of the anterior chamber is presented. The chamber angle is formed by cleavage of uveal tissue to form the iris root, trabeculum, and ciliary body. When cleavage is incomplete or faulty, uveal tissue is adherent to the trabecular zone. The development of congenital glaucoma is related to this faulty cleavage, rather than to persistent mesodermal remnants. (10 figures, 8 references) G. S. Tyner.

Allen, L., Burian, H. M., and Braley, A. E. **The anterior border ring of Schwalbe and the pectinate ligament.** A.M.A. Arch. Ophth. **53**:799-806, June, 1955.

Prominent anterior border-rings of Schwalbe and pectinate ligament features in man are the result of excessive laying down of mesodermal tissue in embryonic and fetal eyes. They do not result from a failure of atrophy and resorption of mesodermal tissue normally laid down in each embryo.

Comparative anatomic studies show that analogies to all forms of pectinate fiber anomalies occurring in man are found in the normal chamber angles of animals. In man they represent genetically determined atavistic traits. (5 figures, 4 references) G. S. Tyner.

Burian, H. M., Braley, A. E., and Allen, L. **Visibility of the ring of Schwalbe and the trabecular zone.** A.M.A. Arch. Ophth. **53**:767-783, June, 1955.

Schwalbe's line and the trabeculum can be seen by slitlamp examination as a "golden glow in the region of the chamber angle." A narrow beam is used on the sclera at the temporal or nasal limbus. In some eyes the line is more prominent than normal. This prominence is due to an "excessive laying down of cells and excessive relative growth." The term embryotoxon which refers to a hyalinization of this area should be discarded since there is no hyaline membrane. Prominence of the ring may be associated with but not necessarily related to glaucoma and some congenital anomalies such as polycoria and corectopia. (12 figures, 22 references) G. S. Tyner.

François, J., Neetens, A. and Collette, J. M. **Ocular microangiography.** Ophthalmologica **129**:145-159, March, 1955.

Microangiography as used by the authors is a form of microradiography, that is, the visualization by roentgenography of tissue elements or tissue channels into which radio-opaque materials can be injected. The method has proved particularly fruitful in the study of vascular systems as a whole, particularly that of the kidney. Application of the method to the human eye has revealed important findings. Retinal and optic nerve capillaries anastomose in the peripapillary zone of the retina. The intraocular branches of the posterior ciliary arteries supply only the choroid. The major circle of the iris has no connections with the arterial system of the choroid (19 figures, 18 references. Peter C. Kronfeld.

Genis-Galvez, Jose M. **The innervation of the lacrimal canaliculi.** Arch. Soc. oftal. hispano.-am. **15**:71-85, Jan., 1955.

This is a report of a histologic study of the innervation of the lacrimal canaliculi, the material comprising the lids of 20 adult cadavers, fixed in formalin, and sectioned and stained according to the method of Bielschowsky-Gross and its modification by Jabonero. The histologic structure, with emphasis on the innervation, is described in detail. The interesting revelations of this study are the inclusion of fibers of the orbicularis in the walls of the canaliculi, and the presence of an epithelial layer with germinative characteristics and the morphologic picture of desquamation with poorly staining cells, as evidence of low vitality. A dense vascular network in intimate contact with the epithelium was suggestive at times of erectile tissue, similar to that described about the eyelashes. The innervational distribution in the walls of the canaliculus is also similar in type to that which Tello described at the base of the lashes. Corpuscular formations found in the walls of the canaliculi, which the author regards as sensory, appear also to be identical with those described by Tello in the eyelashes. It appears from this study that the canaliculi, the lashes and other lid structures are supplied with an innervation controlling the neurotropic action of epithelial tissues, modified only by its special functional character. (10 figures, 6 references) Ray K. Daily.

Wolter, J. Reimer. **The cells of Remak and the astroglia of the normal human retina.** A.M.A. Arch. Ophth. **53**:832-838, June, 1955.

Using an improved stain, the author has demonstrated various types of astroglia which form a structural supportive network for the retinal neurons and vessels. (13 figures, 12 references) G. S. Tyner.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Smith, C. H. **Bacteriology of the healthy conjunctiva.** Brit. J. Ophth. **38**: 719-726, Dec., 1954.

An attempt is made to determine the normal bacterial flora of the conjunctiva since the advent of antibiotics. The paper reports the investigation of conjunctival findings in 5,000 patients made in 1950-1951. The use of all antibiotics was stopped at least 24 hours before culture and patients that were scheduled for "clean" surgery were the only ones used in this study. Antibiotic sensitivity tests were performed on all potentially pathologic organisms. The author finds a definite change in the flora of the eye and notes a decrease in both pathogenic and nonpathogenic organisms, and feels that this is in part due to the use of antibiotics. Gram-negative bacilli seem to be present to a greater extent and there is some resistance to the antibiotics. The pre-

operative use of streptomycin or polymixin is advised. (5 tables, 10 references)
Lawrence L. Garner.

Witmer, Rudolf H. **Antibody formation in rabbit eye studied with fluorescein-labeled antibody.** A.M.A. Arch. Ophth. **53**:811-816, June, 1955.

Experimental studies indicate that local antibody formation takes place in the inflamed eye after placement of irritants in the vitreous or anterior chamber. (6 figures, 1 table, 9 references) G. S. Tyner.

Wolter, J. Reimer. **Modern neuropathology applied to the eye.** Klin. Monatsbl. f. Augenh. **126**:670-678, 1955.

The author used Hortega's method of silver carbonate impregnation of the retina. Early degeneration of the ganglion cells can be diagnosed. Terminal swelling of nerve fibers (Cajal) can be easily seen. Astrocytes can be found in the retina with this method. (6 figures, 13 references)
Frederick C. Blodi.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Auricchio, G. **Current views concerning the physiology of the intraocular fluids.** Boll. d'ocul. **34**:257-300, May, 1955.

The author very thoroughly reviews the subject under three headings: 1. the present status of the theory of secretion, 2. determination of the outflow-rate of the aqueous humor and 3. the origin of the ascorbic acid in the intraocular fluids. (6 tables, 143 references)
William C. Caccamise.

Bahn, G. C., and Allen, J. H. **Therapeutic studies in experimental chemical injury of the cornea.** A.M.A. Arch. Ophth. **54**:22-27, July, 1955.

Calsulfhydryl had no beneficial effects in treatment of acid burns of the cornea in rats and was thought to be detrimental in some cases of alkali burns of rat's corneas. (2 figures, 9 tables, 2 references)
G. S. Tyner.

Boehringer, H. R., and Schelling, F. **The ascorbic acid content of the aqueous of normal and inflamed human eyes.** Ophthalmologica **129**:275-280, April-May, 1955.

In 52 human subjects with normal eyes the relationship between the ascorbic acid content of the aqueous and that of the plasma was found to be essentially the same as in the rabbit. With rising plasma levels the aqueous level rose sharply to reach a definite plateau at a mean ascorbic acid concentration of 23 mg. percent. The corresponding plasma value was about 1 mg. percent. Further rises of the plasma level were not associated with any significant changes of the aqueous level. This level represents the saturation point of the probably secretory mechanism which is responsible for the transfer of ascorbic acid into the eye. Actually the saturation level may be dependent upon the facilities for secretory transfer minus the facilities for diffusion of ascorbic acid back into the bloodstream.

In 35 human eyes with active uveitis the saturation level was found significantly lower than in normal human eyes. The difference may be due to impaired secretion or improved diffusion. (1 figure, 10 references) Peter C. Kronfeld.

Cooper, S., Daniel, P. M., and Whitteridge, D. **Afferent impulses from the muscle spindles of the extrinsic eye muscles and their course within the brainstem.** Tr. Ophth. Soc. U. Kingdom **74**:435-440, 1954.

The authors' experimental work on monkeys and goats showed that there are proprioceptors of the eye muscles which are of great importance in view of the fine and accurate adjustment that these muscles are required to make in order to con-

trol the movements and maintain the posture of the eyeball. (5 figures, 10 references) Beulah Cushman.

King, J. H., and Weimer, J. R. **Prednisone (meticorten) and prednisolone (meticortelone) in ophthalmology.** A.M.A. Arch. Ophth. **54**:46-54, July, 1955.

These newer steroid preparations proved superior to cortisone or hydrocortisone in most instances. Therapeutic action was more rapid, complications and side effects from use of the drug were fewer. These drugs have the same indications and contraindications as cortisone or hydrocortisone. Favorable therapeutic effects may be gained where the older drugs fail. (3 figures, 5 tables, 9 references) G. S. Tyner.

Marsico, Vincenzo. **Comparative study of some ganglioplegics and their association with regard to their effects on the eye.** Arch. di ottal. **59**:117-133, March-April, 1955.

The following data were observed in 20 normal subjects while they received Elvetil, a ganglioplegic with parasympathetic action and pendiomid or hexamethonium which have a mixed action: arterial pressure of the retinal vessels, ocular tension, pupillary diameter and range of accommodation. No antagonism was observed between the three drugs investigated but only synergism. No essential difference could be found between the effects of pendiomid and hexamethonium. (4 tables, 14 references) John J. Stern.

Quintieri, C. **The diffusion of erythromycin into the intraocular fluids.** Boll. d'ocul. **34**:193-198, April, 1955.

The author studied the diffusion of orally administered erythromycin into the aqueous and vitreous in rabbits. Bacteriostatic levels were obtained in the aqueous when there were adequate blood levels. No trace of the drug could be found in the vitreous, however. Considering the broad antibacterial spectrum, the low toxicity, and the convenience of administration of the drug, the author believes that erythromycin can be usefully employed in ophthalmology. (1 figure, 1 table, 14 references) William C. Caccamise.

Recupero, Cenzo. **Electrophoretic studies of the serum protein in diabetic retinopathy.** Arch. di ottal. **59**:89-102, March-April, 1955.

Fourteen diabetics with retinopathy were examined. In the absence of albuminuria and hepatic lesions there were hardly any alterations of the serum protein distribution; when albuminuria and hepatic lesions were present, severe and constant changes were found: hypoproteinemia, hypoalbuminemia, low gammaglobulin values; more rarely an increase of the alpha-2 fraction, and even more rarely that of the alpha-1 fraction were observed. These disturbances may play a role in the genesis of retinopathy in patients with hepato-renal disturbances. (1 figure, 2 tables, 38 references) John J. Stern.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Allen, Merrill J. **The stimulus to accommodation.** Am. J. Optometry **32**:422-431, Aug., 1955.

The relation of accommodation and convergence to stimuli at 0, 2 and 4 diopters distance was studied by means of a haploscope and two cameras. On one film, the separation of Purkinje images indicated accommodation, while on the other the usual ophthalmograph lines were recorded. The results on one subject were discussed in regard to Fincham's theory that the accommodation is triggered principally by chromatic aberration and the Stiles-Crawford effect. Fluctuations of

accommodation occurred which were not accompanied by fluctuations of convergence. Paul W. Miles.

Boehme, G. **Excentric fixation and the treatment of amblyopia.** Klin. Monatsbl. f. Augenh. **126**:694-719, 1955.

Excentric fixation is first discussed in a general way. Central fixation is foveolar, excentric fixation may be foveal, juxtafoveal or peripheral. This fixation must be tested uniocularly with the good eye covered. Its situation depends mainly upon the degree of amblyopia, but the motor conditions of the eye (ductions) also play a role.

The treatment is important, as the excentric fixation seriously complicates amblyopia. The routine used at Bangerter's clinic in Switzerland is outlined. With success, a retinal chamber of Nordenson is used. The carbon-arc guarantees a high light intensity; the central ophthalmoscope enables one to observe the fundus carefully; a high variability in the degree of light intensity is possible. The extrafoveal area is dazzled with bright light so that this area becomes inactive and refractory. At the same time the central area is stimulated with small colored figures.

Among 160 patients with amblyopia 66 had excentric fixation; 75 percent of the excentric fixations had a more or less stable central fixation after a course (44 sessions on the average) of orthoptic treatments. (17 references)

Frederick C. Blodi.

Burian, H. M., and Allen, L. **Mechanical changes during accommodation observed by gonioscopy.** A.M.A. Arch. Ophth. **54**:66-72, July, 1955.

Slitlamp gonioscopy revealed changes in position and contour of structures of the anterior segment of the eye during accommodation which tend to support the Helmholtz theory. Some of the observations were forward movement of the pupillary margin, backward bowing of the middle third of the iris, change in contour of the trabecular zone, and change in contour of the lens. (6 figures, 3 references) G. S. Tyner.

Ehrich, Wulf. **Diagnosis and importance of various types of fixation in amblyopia.** Klin. Monastbl. f. Augenh. **126**:720-727, 1955.

The type of fixation in the amblyopic eye can be ascertained with an ophthalmoscope (small aperture) while the good eye is covered. The patient is asked to fixate and follow the ophthalmoscope light and the examiner sees the area of fixation in the fundus. The following types are distinguished: 1. changing excentric fixation and occasional macular fixation (type without fixation of Bangerter), 2. excentric, paramacular and parafoveolar fixation (pseudomacular) and 3. true macular fixation.

A combination of occlusion and orthoptic treatment is advised. Ten patients out of 45 were converted to stable central fixation; all of them belonged originally to type 1. Results in group 2 were poor or dubious. (2 tables, 9 references)

Frederick C. Blodi.

Harata, M. **Analysis of the light sense by eyeball compression.** Acta Soc. Ophth. Japan **59**:455-457, May, 1955.

The light sense disappears during compression of the eyeball. The author was the subject of the first experiment. The eyeball was compressed by an ophthalmodynamometer until the light of the Nagel adaptometer disappeared. Greater pressure was required to extinguish the light sense when the brightness of the object was increased. In one case of achromatopsia, the same result was obtained. In this condition, therefore, the function of the rods must be normal, as has been generally accepted. In cases of pigmen-

tary degeneration of the retina, the result was similar, but a smaller compression was enough to extinguish the light sense. In all of these cases the status of adaptation showed no relation to the necessary intensity of the compression. After light adaptation the brightness of the object looked darker. Nevertheless, the same compression was required as before to extinguish the light sense. The author finally concludes that the required intensity of the compression may give an indication of the impulse intensity of the light sense. (1 figure, 1 table, 5 references)

Yukihiko Mitsui.

Jayle, G. E., and Berard, P. V. **Perimetry in high myopia.** Ann. d'ocul. **188**: 431-452, May, 1955.

Visual field examinations on 100 myopic eyes (without correcting lenses) using the Goldmann perimeter and the weakest possible test stimuli are reported. In 76 percent of the cases the results could be classed as typical: normal fields, enlargement of the blind spot, sometimes breaking through temporally, with or without involvement of the fixation area. In 24 percent of cases the defects were atypical: enlargement of the blind spot breaking through nasally, cecocentral scotoma, ring scotoma and hemianopic defects. In many cases relative scotomata occurred in the absence of visible chorioretinal lesions in the corresponding area of the fundus. 26 eyes were studied to determine what effect the wearing of correcting lenses had on these field changes. The results of this study were variable. The significance of the findings are discussed. (16 figures, 9 tables)

John C. Locke.

Junceda Avello, J. **The determination of visual acuity.** Arch. Soc. oftal. hispanoam. **15**:184-205, Feb., 1955.

After a comprehensive review of the factors affecting the results of visual acuity tests, the author classifies the variables of the emmetropic eye in two groups: those caused by the dioptrics of the eye, and those rooted in the retina and the nervous system. Those dependent on the optical system of the eye include the size of the test types, the illumination, contrast, size of the pupil, and aberrations of the eye. The factors associated with the retina and nervous system are exposure time, and psychologic factors, such as attention, fatigue, and glare. The following requirements as essential for an accurate test: 1. preparation of the patient by seating him for 15 minutes, with eyes open and without reading in a room illuminated by 40 candles of indirect light free of reflexes, 2. avoiding the instillation of any drugs into the eyes prior to the test, 3. testing the patient in a dark room, at a distance of five meters from the test types, 4. the use of white test types on a dull dark background, arranged not in lines but in groups, using animals for children and illiterates, and 5. the use of a projector for the projection of the optotypes on a white screen with a high coefficient of reflection (80 percent). The types should be projected with a light free of ultraviolet rays, and enriched with yellow light corresponding to sodium rays of 5,880 Å. A scale for the size of letters, based on the tangent of the visual angles, is submitted. The test type should be exposed for no longer than one minute. For the sake of uniformity, the visual acuity should be recorded in decimals of normal acuity. (13 figures, 35 references)

Ray K. Daily.

de Leonibus, Fernando. **Investigations on the spherical aberration of the cornea.** Arch. di ottal. **59**:77-87, March-April, 1955.

Using a method proposed by Gullstrand, the author has confirmed on four human eyes what Gullstrand had found in one, namely that a more or less marked posi-

tive spherical aberration is present in different sectors and different subjects. Only the central (optical) part or even only a sector of it has spherical correction (or overcorrection) which, however, almost never extends into the periphery. (1 figure, 4 tables, 7 references)

John J. Stern.

Miles, Paul W. **Optics and visual physiology.** A.M.A. Arch. Ophth. **53**:893-914, June, 1955.

The literature for 1954 is reviewed. (278 references) G. S. Tyner.

Piper, Hans-Felix. **Congenital gaze palsy as a fixation of primitive functions.** Klin. Monatsbl. f. Augenh. **126**:731-739, 1955.

In children the gaze upward is better developed than the gaze downward. This primitive defense mechanism may be maintained and give rise to various gaze palsies. Three cases are mentioned which could perhaps be explained on such a basis. (10 figures, 1 table, 12 references)

Frederick C. Blodi.

Roelofs, C. O., and Zeeman, W. P. **Apparent size.** Ophthalmologica **129**:166-186, March, 1955.

The apparent size of an object is related to 1. the size of the retinal image, 2. the actual as well as the apparent distance between object and observer, 3. familiarity with the actual size of the object, and 4. the presence of familiar objects of comparison. The present study concerns itself with size judgments of luminous, diamond-shaped objects, placed, with the help of mirrors, at distances from 3 to 27 meters and viewed by the observer monocularly or binocularly, with and without familiar comparison objects.

Under conditions of binocular observation in the dark, size constancy prevailed up to a distance of 4.5 meters. At distances from 4.5 to 26.6 meters the apparent size of the object decreased at a lesser rate than the size of the retinal images. At still greater distances the apparent size decreased at the same rate as the retinal image. The authors conclude that the convergence impulse influences both apparent size and apparent distance, but this does not prevent both magnitudes from being altered by a number of other factors. (4 tables, 13 references) Peter C. Kronfeld.

Salleras, Alejandro. **Correction of large ametropias and anisometropias through the inclusion of acrylic lenses into the anterior chamber. Report of four cases.** Arch. oftal. Buenos Aires **30**:43-58, Jan., 1955.

In an attempt to overcome the difficulties inherent in, and the main pitfalls of, the insertion of a Ridley lens behind the iris diaphragm, with which technique satisfactory results had been obtained previously in only 9 of 25 cases, the author resorted to Strampelli's operation, which consists of introducing a small, tripronged acrylic lens of an adequate refractive power between the cornea and the iris through a narrow limbal incision (cf. Strampelli, B.: Ann. di ottal. 80:75-82, 1954).

Four patients were operated upon, three of them aphakics, in whom an extracapsular cataract extraction had been performed previously, and one a patient who having had a corneal transplant made because of an adherent leucoma, remained with a compound myopic astigmatism. While the immediate postoperative course was on the whole uneventful, late complications appeared in the form of pigmentary deposits, corneal edema or displacement of the lens. Preoperative corrected vision was consistently better than the uncorrected postoperative one. Thus, in the first two cases it went from 20/20 to 20/100, in the third from 20/25 to 20/100 and in the fourth from 20/20 to 4/100. No information is given with respect to the

eventual recovery of binocular vision; this, however, may be regarded as the only, or at least the chief reason to be adduced in favor of such a procedure. (9 figures, 2 references)

A. Urrets-Zavalia, Jr.

Schmidt, Ingeborg. **A sign of manifest heterozygosity in carriers of color deficiency.** Am. J. Optometry **32**:404-408, Aug., 1955.

This is a discussion of a theory of color vision and color blindness modified by Schmidt's discovery that carriers of color defects may have normal color vision but an abnormal spectral luminosity curve. Wall's theory of the contribution of cones which are sensitive to red, green and blue to general brightness sensation is fully described. The heredity data derive from a study of 35 carriers of protanomaly, protanopia, deuteranomaly and deuteranopia.

Paul W. Miles.

Young, Francis A. **An evaluation of the biological and nearwork concepts of myopia development.** Am. J. Optometry **32**:354-366, July, 1955.

The etiology of myopia should be studied in the same manner as intelligence. The importance of heredity and nearwork should be determined in identical twins put to different types of visual work. The Steiger theory that myopia is a chance coincidence of various structural eye factors each of which has a normal variation in the population is criticized. By the same reasoning, one could prove that the type of car you buy is purely a matter of chance.

Paul W. Miles.

5

DIAGNOSIS AND THERAPY

Alfano, J. E., and White, H. **The ocular significance of intracranial calcium deposits.** A.M.A. Arch. Ophth. **54**:77-91, July, 1955.

Numerous illustrations of the value of X-ray studies of the skull in differential diagnosis of related ophthalmological problems are presented. Intracranial calcifications may be noted in toxoplasmosis, Sturge-Weber syndrome, tuberous sclerosis, a variety of tumors and vascular anomalies which affect the ocular apparatus. Such studies may in some instances be invaluable. (31 figures, 14 references)

G. S. Tyner.

Barraquer, Thomas. **Perforating autokeratoplasty.** Arch. Soc. oftal. hispano-am. **15**:292-294, March, 1955.

To facilitate the transposition of corneal segments, the author devised an instrument which is introduced into the anterior chamber and held against the posterior surface of the cornea, blocking the two corneal openings until the operation is completed. It consists of a quadrangle attached to a handle, ending at the opposite end in a sharp triangular knife. The entire instrument resembles a keratome. After the segments to be transposed are outlined with the trephine, their outlines made distinct by staining, and the sutures introduced, the instrument is inserted like a keratome at the limbus, pushed across the anterior chamber and anchored in the angle of the anterior chamber on the opposite side. It is then held there by an assistant until the operation is completed. (2 figures)

Ray K. Daily.

Belmonte Gonzalez, Jose. **An improvement in the biomicroscopy of the periphery of the fundus.** Arch. Soc. oftal. hispano-am. **15**:287-289, March, 1955.

Finding that the Hruby lens does not give adequate access to the periphery of the fundus, the author designed an attachment to the Zeiss slitlamp by means of which the Goldmann contact lens for the fundus may be held in front of the cornea in the same manner as the Hruby lens. With the pupil well dilated this arrange-

ment permits inspection of the peripheral portions of the fundus. (2 figures)
Ray K. Daily.

Belmonte Gonzalez, Nicolas. **The evaluation of ophthalmodynamometric data.** Arch. Soc. oftal. hispano-am. **15**:262-264, March, 1955.

The author points out the importance of acquiring an accurate technique with the apparatus used and of determining what is normal with a particular instrument before attempting to evaluate ophthalmodynamometric procedures. Using two tonometers of different manufacture, two different ophthalmodynamometers, and two different sphygmomanometers the author obtained data which lent themselves to almost any desired interpretation. (7 references) Ray K. Daily.

Brégeat, P., and Juge, P. **Acuity and field defects of psychogenic origin. The Maxiton diagnostic test.** Ann. d'ocul. **188**: 334-343, April, 1955.

In visual impairment of psychogenic origin, the fields are usually sufficiently characteristic to make a correct diagnosis possible. Concentric contraction of extreme variability is the most characteristic change, although sector defects and central scotomata may also occur. Incessant blinking, rapid fatigue, and difficulty in maintaining fixation are usually noted. Differentiation is mainly from optochiasmatic arachnoiditis, chiasmal lesions in general, and lesions causing increased intracranial pressure.

The Maxiton diagnostic test gives added support to the diagnosis. One or two ampoules of Maxiton in 20 cc. of physiological serum injected intravenously cause increased emotivity, anguish, malaise, and occipital headache. Visual acuity and fields usually show a spectacular recovery. It is helpful to have warned the subject that if the improvement is not sufficient, the dose will be doubled or tripled. John C. Locke.

Currie, J. D. **Post-operative ophthalmic care.** Tr. Ophth. Soc. U. Kingdom **74**:457-468, 1954.

When the patient is a child, the patient as well as the parents should have a clear conception of what may be expected from surgery, for example, that in glaucoma the field lost will not be regained, and that a squint operation is not the end of the treatment. Detachment operations are not always successful. Beulah Cushman.

Dreisler, Knud K. **Sterilization of tonometers.** A.M.A. Arch. Ophth. **53**:860-864, June, 1955.

A method and instrument for flame sterilizing a tonometer in ten seconds is described. No harm is done to stainless steel tonometers. (2 figures, 4 references)
G. S. Tyner.

Everett, William G. **A new scleral shortening operation.** A.M.A. Arch. Ophth. **53**:865-869, June, 1955.

The operation consists of folding the sclera outward in contrast to the present lamellar resection technique. After decompression of the globe a scleral incision is made and the choroid separated from the sclera with a spatula. The portion of separated sclera is tucked outward and maintained with mattress sutures. (5 figures, 3 references) G. S. Tyner.

Harrington, D. O., and Hoyt, W. F. **Ultraviolet radiation perimetry with monochromatic blue stimuli.** A.M.A. Arch. Ophth. **53**:870-881, June, 1955.

Monochromatic blue test objects are of more value in demonstrating early conduction defects than the standard blue targets. Monochromatic colors are obtained by the use of ultraviolet light and luminescent inks. (22 figures, 8 references) G. S. Tyner.

Hegner, H. J. **A new muscle balance test.** Tr. Ophth. Soc. U. Kingdom **74**:411-421, 1954.

The author developed an instrument (co-ordimeter) with a Maddox rod to be used wth a standard head posture. He measured first the field of binocular fixation and found its limit to be very close to a circle of 50°. He concluded that the 30° circle lies in a position peripheral enough to reveal very fine muscle balance defects. (7 figures) Beulah Cushman.

Heydenreich, A. **The simplified light sense examination of Comberg as a clinical test.** Klin. Monatsbl. f. Augenh. **126**:620-625, 1955.

This is a comparative and a direct, quantitative test. In the first one the light sense in the poorer eye is compared with that of the good eye. In the second test the dark adapted eye is exposed to a light at various distances. During both tests the lids must be closed. This increases the diffusion of light. (2 references)

Frederick C. Blodi.

Hirsch, Monroe J. **An evaluation of scleral tonometry. Its reliability, validity and clinical applicability.** Am. J. Optometry **32**:391-403, Aug., 1955.

The reliability, validity and the clinical applicability of the Wolfe tonometer receives attention in this paper. The tension was determined in every patient over the age of thirty years in one series and over forty in another series, for a total of 152 eyes. The test seemed to be reliable if repeated readings were taken and the first ones discarded. The instrumental error formerly believed to be as high as 7 mm. is here determined as about 5. One patient had a subconjunctival hemorrhage as a result of the test. Scleral tonometry is modified greatly by differences in scleral rigidity, causing a skew in a statistical series not present for corneal tonometry. It should not be considered an absolute screening device for glaucoma.

Paul W. Miles.

Klein, M. **Eye drops and pyocyanea.** Tr. Ophth. Soc. U. Kingdom **74**:479-491, 1954.

Methods to avoid contamination of eye drops and droppers are discussed. It is suggested that in commercial preparations of eye drops the composition of the vehicle should be displayed and eye drops should be dated and not used for longer than four weeks from date of issue. (8 figures, 9 references)

Beulah Cushman.

Malbrán, J., and Nunziata, I. **General anesthesia in ophthalmic surgery.** Arch. oftal. Buenos Aires **30**:59-69, Feb.-March, 1955.

Based on their considerable experience (5,048 operations, of which 85 percent were in children, with no mortality), the authors advocate the use of ether-ethyl chloride or of nitrogen monoxide in an open or semi-open circuit in children under the age of three years. In older patients preference is given to pentothal, in association with decamethonium iodide. A balanced general anesthesia, as recommended by Laborit, has proved satisfactory in cataract and corneal surgery, where a depressive action upon the intraocular pressure is particularly desirable.

Respiratory control is effected by means of a stethoscope adapted to a pharyngeal cannula, through which oxygen is administered continuously. On the whole, the practice of tracheal intubation is discouraged as unnecessary and even harmful. (13 references)

A. Urrets-Zavalia, Jr.

di Martino, C. **The therapeutic use of Propiofil in ophthalmology.** Arch. di ottal. **59**:145-153, March-April, 1955.

Propiofil is a proprietary drug which

contains 5 percent sodium propionate and 0.5 percent chlorophyll. It was used in 100 patients with various conditions ranging from simple catarrhal conjunctivitis to herpetic keratitis, and from spring catarrh to allergic blepharoconjunctivitis. The results were encouraging. (28 references) John J. Stern.

Monjé, Manfred. **The examination of squint cases with anaglyphic images.** Klin. Monatsbl. f. Augenh. **126**:586-598, 1955.

Anaglyphic images are produced by a red-green target seen through red-green spectacles. Such a stereoscope was designed by the author. The trial frame is suspended horizontally and the targets lie at 30 cm. distance on the table or are projected at 1 meter. This type of stereoscope is simple and inexpensive. It is useful to determine suppression scotomas, normal or abnormal retinal correspondence and single binocular vision. Fusion and depth perception can be tested with appropriate targets. Orthoptic exercises can also be performed. (3 figures, 26 references) Frederick C. Blodi.

Montouroy, R. **Results of treatment in forty cases of ocular tuberculosis.** Ann. d'ocul. **188**:453-461, May, 1955.

In 40 cases of ocular tuberculosis streptomycin, isoniazid, or P.A.S. were given alone or in combination by various local and systemic routes. When the lesions appeared stabilized, tuberculin therapy was given to reduce the allergy and methylic antigen to increase the immunity. In 19 cases the patient was cured, in 8 improved, and in 13 treatment failed. (21 references) John C. Locke.

Palomar Collado, F. **Pyrazolin derivatives in ophthalmologic therapy.** Arch. Soc. oftal. hispano-am. **15**:113-135, Feb., 1955.

The chemical composition, pharmacology, therapeutic action, mode of therapy, dosage and therapeutic indications in ophthalmology of irgapyrin, which contains 15 percent of sodium butazolidin and 15 percent of pyramidon are reviewed. On the basis of an experience in 55 cases of various ocular diseases, 15 of which are briefly reported, the author concludes that irgapyrin is a powerful addition to the ophthalmologic armamentarium, which provides an anticongestive anti-inflammatory antirheumatic, and analgesic effect. The intensity and rapidity of action are sometimes spectacular. The results obtained are stable and the author encountered no recurrences which could not be attributed to inadequate treatment. While it is not a drug free of danger, the author has not encountered any serious complications, immediate or late, when using the indicated precautions. The blood picture should always be watched when injections of irgapyrin are administered for longer than ten days. The therapeutic action is superior and more enduring than that of most antirheumatic drugs. (21 references) Ray K. Daily.

Philips, A. S., and Hansell, P. **Keratography.** Tr. Ophth. Soc. U. Kingdom **74**:207-213, 1954.

Fincham's application of Amsler's method is described and its value in the diagnosis of keratoconus and cornea plana and in the evaluation of the result of corneal grafting is shown. (9 figures) Beulah Cushman.

Quintieri C. **The practicability of depopenicillin in ophthalmology.** Boll. d'ocul. **34**:301-306, May, 1955.

The author compares the penetration of penicillin into the aqueous of rabbits after the drug has been given intramuscularly both as the depo-form and as the crystalline form dissolved in saline. His results indicate that penicillin dissolved in physiologic saline is undoubtedly the more certain form for treatment in ocular infec-

tions. The use of depo-penicillin would seem to be reserved for prophylaxis. (4 figures, 6 references)

William C. Caccamise.

Riegelman, S., Vaughan, D. G., Jr., and Okumoto, M. **Evaluation of the sporicidal activity of Post's sterilizing solution.** A.M.A. Arch. Ophth. **53**:847-851, June, 1955.

This solution was found to be non-sporicidal when evaluated by the authors. (7 references) G. S. Tyner.

Rosner, Robert S. **New germicidal tonometer stand.** A.M.A. Arch. Ophth. **53**:889-890, June, 1955.

A tonometer stand is described in which ultraviolet radiation ozone is used for sterilizing the foot plate. (1 figure, 1 reference) G. S. Tyner.

Vanysek, J. **Pathology of the electroretinogram.** Ophthalmologica **129**:186-201, March, 1955.

Most workers in the field of electroretinography make the distinction between normal and pathologic electroretinograms (ERG) largely on the basis of the amplitude of the b wave. The present writer doubts the reliability of this criterion, on the grounds that the b wave is made up of the electric responses of a retinal area in which the ratio of affected to unaffected portions may vary within wide limits. Besides, a retinal disease may cause inhibition as well as stimulation of retinal activity. The present writer stresses the diagnostic value of a prolonged latent period (greater than 0.08 seconds), a prolonged, drawn-out b wave (longer than 0.2 seconds) and of a low fusion frequency of flicker stimuli. (14 figures, 26 references)

Peter C. Kronfeld.

Williamson-Noble, F. A. **Post-operative ophthalmic care.** Tr. Ophth. Soc. U. Kingdom **74**:449-455, 1954.

Psychosomatic medicine is an important concept in ophthalmology. It seems probable that if an anxious state of mind can bring about a breakdown of epithelium sufficient to produce a peptic ulcer, it could also cause interference with healing of a cataract section.

The first dressing after cataract extraction should be done one to four days afterwards by a surgeon wearing a face mask. Sterilized sticks, wound with cotton at one end, should be used to remove mucus and the same type of dressing applied as used before. Dark glasses may be worn from the fourth day onward in uncomplicated cases. Corneoscleral sutures should be removed by the tenth day. Glasses are to be ordered a month after surgery. (1 figure) Beulah Cushman.

Young, J. Horton. **Magnetic intraocular implant. New surgery of the implant—the magnetic artificial eye.** Brit. J. Ophth. **38**:705-718, Dec., 1954.

A magnetic buried implant and a magnetic prosthesis has been designed for limited and special application for those globes wherein the area anterior to the anterior attachments of the extrinsic rectus muscles is reasonably intact. The procedure is not suitable in small children or in cases where the rectus or its scleral attachment is not intact.

The author presents a detailed description of the surgical technique which should be reviewed in its entirety by the ophthalmic surgeon, inasmuch as it consists of an extensive anterior preparation followed by a posterior sclerotomy and evisceration. The magnetic implant is then inserted through the posterior sclerotomy incision and sutured to the scleral shell. The placement of sutures in this procedure is vital to the end results and, unless one is meticulous, the results could be disastrous. The patient is kept in bed for 10 days and may use the bathroom on the seventh day. Apparently considerable con-

junctival swelling occurs inasmuch as a prosthesis cannot be fitted until two months have elapsed. (6 figures, 3 references) Lawrence L. Garner.

6

OCULAR MOTILITY

Bangerter, A. **Some indications for orthoptic treatment.** Ophthalmologica **129**: 237-240, April-May, 1955.

For the treatment of severe amblyopia with eccentric fixation Bangerter recommends a type of exercise that consists of stimulation of the true fovea and simultaneous exclusion of the pseudofovea. This is accomplished with an especially designed instrument similar to Gullstrand's ophthalmoscope which produces appropriate stimuli for the fovea and blinding, well-localized stimuli for the pseudofovea. By means of systematic exercises with this instrument (called "pleoptic" exercises by the writer) good to normal visual acuity has been obtained in 25 percent of the cases of severe amblyopia with eccentric fixation.

Unilateral myopia of severe degree may justify extraction of the lens in order to make binocular vision possible. In cases of bilateral myopia of severe degree Malbran's reinforcement operation, utilizing fascia lata combined with scleral resection, should be considered. In cases of paralytic strabismus, correction through natural developments occurs during the first three months, if ever. During these three months intensive orthoptic exercises are indicated. If there is no improvement at the end of three months, surgery is indicated and should consist of O'Connor's muscle plastic, combined with tucking of the paralyzed muscle. A tenotomy of recession of the antagonist is indicated only in cases of extreme secondary contracture. Peter C. Kronfeld.

Hartmann, Edward. **Operative indications in strabismus.** Ann. d'ocul. **188**:397-415, May, 1955.

An early operation is advisable. The choice of muscle varies with different operators. Any anomaly of the muscular insertions or check ligaments must be corrected first. Otherwise one can either weaken the overacting muscles or strengthen their antagonists. A bilateral operation is usually preferable. A unilateral one is sometimes indicated in patients with amblyopia and in strictly cosmetic operations. If a vertical deviation is large, it should be corrected first. Otherwise it is better to deal first with the horizontal deviation. The amount of recession and resection is difficult to assess. Figures vary with different operators and, in any case, are only averages. Each case must be evaluated individually, both clinically and according to the condition of the muscle found at the time of operation. (32 references)

John C. Locke.

Hugonnier, R., and Douthwaite, C. M. **The present status of orthoptics. Its possibilities and limitations.** Ann. d'ocul. **188**: 416-430, May, 1955.

From the point of view of diagnosis, an orthoptic examination is always indicated to evaluate the exact status of binocular vision. As far as treatment is concerned, orthoptics cannot reduce a constant angle of squint. It cannot create fusion where this does not exist, and attempts to do so may result in a tenacious postoperative diplopia. It cannot correct anomalous retinal correspondence. Paralytic strabismus and constant concomitant divergent strabismus are not helped by orthoptics. Esophoria (unless associated with a convergence insufficiency) responds poorly, and hyperphoria and cyclophoria not at all.

By itself, orthoptics can cure most patients with convergence insufficiency, and it can eliminate symptoms in a large num-

ber of decompensated exophorias and in esophoria with associated convergence insufficiency. Accommodational convergent strabismus can sometimes be cured (in association with refractive correction) if the angle of deviation is not excessive and not constant. Some cases of intermittent divergent strabismus of small angle can also be cured.

In association with surgery, orthoptics is helpful in intermittent divergent strabismus, and in convergent strabismus when the angle is less than 25 degrees and fusion exists at the objective angle. Preoperative treatment aims to improve fusional amplitude, eliminate suppression, and establish diplopia. Postoperative treatment aims for further improvement in fusional amplitude.

The number of sessions should never be over twelve. Orthoptics should not be attempted unless the corrected vision in the two eyes is nearly equal.

John C. Locke.

Jimenez Munoz, R., and Vela Barca, A. **A case of exophthalmic ophthalmoplegia.** Arch. Soc. oftal. hispano-am. **15**:180-183, Feb., 1955.

The author reports a mild case of this disease, in a woman 51 years old, who improved after a month of medical therapy which included estrogens. The etiology, clinical cause and therapy of the disease are briefly discussed. (8 references)

Ray K. Daily.

Murray, Robert G. **The diagnostic significance of restricted ocular motility in children.** J. Neurosurg. **12**:278-286, May, 1955.

The records of 122 patients under 16 years of age with acquired disturbance of ocular motility are analyzed. Patients with 1. a congenital abnormality of development that affected ocular motility, 2. with proptosis and a retrobulbar mass which presumably interfered locally with the function of the nerves or muscles and 3. those who had poliomyelitis were excluded from the study. Intracranial tumors were found in over 70 percent of the children and the mortality rate was 70 percent at the time of writing. This grave implication of an acquired disturbance of ocular motility in children emphasizes the obligation to study each patient exhaustively. The generally accepted belief that paralyses of the sixth nerve are caused by increased intracranial pressure per se is challenged. Other causes of the paralysis are described and it is shown that paralysis of the sixth nerve may have localizing value. (7 tables, 2 references)

F. H. Haessler.

Quereau, J. V. D. **Rolling of the eye around its visual axis during normal ocular movements.** A.M.A. Arch. Ophth. **53**:807-810, June, 1955.

The author believes from his experiments that there is no rolling (true torsion) when the eyes move vertically or horizontally from the primary position. Rolling was noted only in oblique movements of the eye. (2 figures, 2 references)

G. S. Tyner.

Steiger, R. M., and Wuerth, A. **The evaluation of squint amblyopia by means of fixation photography and electroencephalography.** Ophthalmologica **129**:240-244, April-May, 1955.

Fixation photography is a method for the accurate determination of the retinal area used for fixation. The instrument used for this purpose is a fundus camera into which, at the plane of the first real retinal image, a target for fixation has been inserted. The examinee sees this target considerably enlarged by the optical system of the ophthalmoscope and fixates upon it. A fundus photograph taken at this moment shows a sharp picture of the target superimposed upon the picture of the eyeground. The location of

the target within the eyeground defines the retinal area used for fixation.

Utilizing this method, the cases of amblyopia with eccentric fixation may be divided into two groups: 1. cases with eccentric but stable fixation in the sense that more or less the same retinal area is consistently used for fixation, and 2. cases with such extreme variations of the retinal area used during the test that one can hardly speak of "fixation." The average visual acuity was the same in the two groups. The response to orthoptic treatment was fairly good in the cases of the first group and unsatisfactory to nil in the cases of the second group. Fixation photography thus proved to be of prognostic value. Electroencephalography which the authors had included in their workup of cases of strabismus only recently, gave a pathologic result in less than 20 percent of their cases. (4 figures)

Peter C. Kronfeld.

Wheeler, Maynard C. **Strabismus.** A.M.A. Arch. Ophth. **54**:100-134, July, 1955.

The pertinent literature for the year is reviewed. (128 references) G. S. Tyner.

7

CONJUNCTIVA, CORNEA, SCLERA

Albert, P., and Aznarez, J. **Neuroparalytic keratitis with recovery.** Arch. Soc. oftal. hispano-am. **15**:274-286, March, 1955.

The literature on neuroparalytic keratitis, following operations for the relief of trigeminal neuralgia is reviewed, and two cases with favorable outcome are reported. The author believes that the disease is a manifestation of a trophic disturbance in the sympathetic innervation of the cornea and points out that it does not occur after Dandy's operation. The therapy recommended is internal administration of vitamin B and vitamin A. Terramycin is administered to combat infection. Hourly instillation of sterile physiologic solution is made to prevent dryness of the cornea and noviform, atropine and dionin ointment are applied freely. The eye is kept patched between applications. In the two cases reported the patients recovered, one with a visual acuity of 1/7, and the other with 1/4. (11 references)

Ray K. Daily.

Babel, J., and Bourquin, J. B. **Intracorneal transplantation of sclera.** Ophthalmologica **129**:224-230, April-May, 1955.

This is a clinical and histologic study of various processes which take place in rabbit eyes the corneas of which had been made the recipients of interlamellar, homologous and heterologous, scleral implants. In contradistinction to the findings of Winkelman (Am. J. Ophth. 34:1379, 1951) the grafts underwent no major structural change except for a slight degree of absorption. (7 figures, 12 references)

Peter C. Kronfeld.

Bellavia, Marco. **A case of mosaic dystrophy of Bowman's membrane.** Arch. di ottal. **59**:134-144, March-April, 1955.

A case of bilateral mosaic dystrophy in a young woman which had appeared after an attack of keratitis of unknown origin eight years previously, and who in addition presented bilateral cataracts, is reported. After cataract extraction a corneal opacity remained which indicated a dystrophic predisposition of the cornea. In the classification suggested by the author in Bologna during the Italian Congress of Ophthalmology, the condition is classified under paragraph b of the second type of the second group of non-inflammatory corneal processes. (1 figure, 10 references)

John J. Stern.

Buerki, E., and Rohner, M. **A rare case of crystalline corneal dystrophy.** Ophthalmologica **129**:211-217, April-May, 1955.

To the few cases of crystalline corneal dystrophy in the adult reported in the literature, the present writers add another one. A 50-year-old Swiss woman with negative family history showed fine crystalline deposits practically throughout both corneas, causing slight photophobia but no functional impairment. No deposits could be seen in the conjunctiva. General physical examination revealed bilateral contracture of the palmar aponeurosis (Dupuytren), slight acceleration of the blood sedimentation, and a slightly higher than normal amino acid content of the urine. (7 figures, 26 references)

Peter C. Kronfeld.

Cagianut, B. **The substrate of the Kayser-Fleischer corneal ring.** Ophthalmologica **129**:218-219, April-May, 1955.

In two typical cases of Wilson's pseudosclerosis with corneal rings, the writer had the opportunity of making post-mortem histochemical examinations of the corneas. The pigment that made up the ring proved to be soluble in mineral acids, but not in alkali. By spectroscopy silver, copper and nickel could be demonstrated. Since copper was found in normal corneas and since the patients had not received any silver medication, the writer attached significance to the finding of silver in the cornea. Systemically both cases showed signs of disturbed protein and copper metabolism. Peter C. Kronfeld.

Koenig, H., and Marty, F. **A new solvent for calcium deposits in the cornea.** Ophthalmologica **129**:219-224, April-May, 1955.

In three cases of bandshaped keratopathy the writers obtained good results with topical applications of ethylene-diamino-tetra-acetic acid, the agent first recommended for dissolving calcium deposits in the cornea by Grant (cfr. Arch. Ophth. 48:681, 1952). The epithelium over the affected area is removed and a 0.37 percent solution of the agent instilled repeatedly during a period of 15 minutes. Some of the larger particles may have to be lifted off with a spatula. The residual defect heals within two or three days. (1 figure, 19 references)

Peter C. Kronfeld.

Mann, Ida. **Clinical observations on the prophylaxis of ophthalmia neonatorum.** Brit. J. Ophth. **38**:734-741, Dec., 1954.

The author made a clinical and bacteriologic evaluation of the advisability of prophylactic treatment to the eyes of the newborn. In severe purulent ophthalmia the results were equally good in subjects treated prophylactically by Credé's method as in those whose eyes were cleansed with normal saline. As might be expected, earlier and more profuse sterile discharge was noted in the group receiving silver nitrate. The group of infants treated with silver also were found to show clearing up of conjunctival reaction faster than the untreated control group. All organisms found were tested for antibiotic sensitivity in both groups and streptomycin sensitivity was found in each case. Surprisingly, penicillin and sulfadiazine gave the worst results. The author suggests that streptomycin might be the best prophylactic eye drop and concludes that the use of silver nitrate is correct, but is unnecessary in a modern hospital and in a population where gonorrhea is rare. (1 figure, 6 tables)

Laurence L. Garner.

Popp, Claus. **Superficial punctate keratitis after external drug administration.** Klin. Monatsbl. f. Augenh. **126**:754-756, 1955.

In a tuberculosis sanatorium 14 patients developed a peculiar epithelial keratitis in both eyes with photophobia and decreased vision. The corneal lesions consisted of numerous intraepithelial vesicles. All of the affected patients had been given iso-

niazid and a thiosemicarbazon derivative for several weeks. (1 table, 4 references)
Frederick C. Blodi.

Simpson, D. G. **Ocular pemphigus.** Canad. M.A.J. **72**:921-923, June 15, 1955.

A case of pemphigus of the conjunctiva in an 84-year-old man is reported. The Macht test was positive. The patient was given ACTH. Just when improvement was anticipated, the patient expired. Post mortem examination revealed no signs of pemphigus other than in the conjunctiva. (4 figures, 19 references)
Irwin E. Gaynon.

Thomas, J. W. Tudor. **Fixation of corneal grafts.** A.M.A. Arch. Ophth. **54**:1-5, July, 1955.

Fixation of a corneal graft is an important factor in its ultimate clarity. Accurate apposition of the graft and donor site is obtained in the author's experience by shelving margins, two overlying sutures and covering the cornea with egg membrane. Sutures are left in place 10 to 12 days. The shelving margins are obtained by using a smaller trephine for outlining the graft. (11 references)
G. S. Tyner.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Cassady, J. V., Culbertson, C. S., and Bahler, J. W. **The etiology of retinochoroiditis and uveitis.** A.M.A. Arch. Ophth. **54**:28-36, July, 1955.

The sera of 23 of 36 patients with posterior uveitis were positive for toxoplasmosis when examined by the serum modifying antibody dye test of Sabin and Feldman. Eleven patients improved dramatically when treated with pyrimethamine and sulfadiazine systemically. (2 tables, 39 references) G. S. Tyner.

Dekking, H. M. **Aetiology of chronic uveitis.** Tr. Ophth. Soc. U. Kingdom **74**: 503-508, 1954.

The author reports that one or more possible causes could be found in 40 to 50 percent of all patients with uveitis. (6 references) Beulah Cushman.

9

GLAUCOMA AND OCULAR TENSION

Arruga, H. **Diamox in ophthalmology.** Arch. Soc. oftal. hispano-am. **15**:374-380, April, 1955.

This is a report based on an experience in 58 cases. The conclusions are that the most marked effect is obtained in acute and secondary glaucoma. In chronic inflammatory glaucoma good results may be obtained in 50 percent of cases, particularly in early cases. In chronic simple glaucoma the results are favorable in a majority of cases, and are similar to those obtained with miotics. Diamox is very valuable in the transitory postoperative hypertensions. Absolute glaucoma does not respond to this drug. Diamox is useful in the preoperative preparation of patients with glaucoma, and in cases of glaucoma in which it is desirable to dilate the pupil for an examination of the fundus. (12 references) Ray K. Daily.

Bartolozzi, R., and Garcia-Alix, C. **Diamox in the treatment of glaucoma.** Arch. Soc. oftal. hispano-am. **15**:381-422, April, 1955.

The authors report their experiments with this treatment in 37 cases. The effect of diamox is indicated with graphs in each case. The authors conclude that the effect of diamox is similar to that of a cyclodiathermy. It is indicated in all cases of ocular hypertension. Its principal indication is in narrow angle glaucoma, and particularly in the congestive phases. In open angle glaucoma it is less useful because of its toxicity and progressive

diminution of efficacy. Its association with miotics is indicated because of their different mode of action. It is a valuable preoperative and postoperative agent, and is useful clinically for ophthalmoscopic examination in cases in which pupillary dilatation may produce a rise in ocular tension. (37 graphs, 25 references)

Ray K. Daily.

Flocks, M., Littwin, C. S., and Zimmerman, L. E. **Phacolytic glaucoma.** A.M.A. Arch. Ophth. **54**:37-45, July, 1955.

The term phacolytic glaucoma is proposed for the clinical entity of glaucoma associated with hypermature cataract. The responsible mechanism is leakage of liquified cortex into the anterior chamber. This material excites a histolytic response. Swollen macrophages block the filtration angle. (12 figures, 2 tables, 15 references) G. S. Tyner.

Lorente, J. **Clinical study with diamox. Its action on ocular tension in glaucoma.** Arch. Soc. oftal. hispano-am. **15**:355-373, April, 1955.

A review of the literature is followed by an analysis of the author's experience in 17 cases of secondary ocular hypertension and 14 cases of primary glaucoma. The 17 cases of secondary glaucoma demonstrating the beneficial effect of diamox on the ocular tension are briefly reported. In 14 eyes with compensated glaucoma the response was uniformly favorable. A high ocular tension did not fall to normal but was markedly reduced. The author points out the marked subjective improvement in the patients and their preference for diamox as against miotics. In six cases of acute glaucoma refractory to miotics the response to diamox was dramatic. In chronic cases the effect is less constant. Tension was not reduced in hemorrhagic glaucoma, although there was subjective improvement. The dose of diamox used varied from 125 to 500 mg. daily. (5 graphs, 10 references)

Ray K. Daily.

Marin-Amat, M. **The ciliary body as the site of election for glaucoma surgery.** Arch. Soc. oftal. hispano-am. **15**:423-447, April, 1955.

The author, who is an enthusiastic proponent of the neurovasculatory theory of the pathogenesis of glaucoma, holds that all antiglaucoma operations are effective to the extent to which they bring about an atrophy of the ciliary body, with a consequent restoration of a normal sympathetic and parasympathetic relationship. Anatomically and physiologically the ciliary region is the vital and trophic region of the eyeball, and it contains the center for the regulation of the ocular vascular circulation and innervation. All effective antiglaucoma operations act primarily on the ciliary body. The author takes issue with Weekers, who holds that an iridectomy acts by facilitating intraocular drainage. The author maintains that it acts by diminishing the quantity of blood entering the eyeball and thereby inhibits the secretion of aqueous. He also disagrees with Sourdille, who believes that an iridectomy acts directly on the ocular hypertension. The author believes that it acts on the center regulating the intraocular circulation, and by modifying the circulation and innervation affects the ocular tension indirectly. The filtration action of fistulating operations the author regards as an auxiliary action in cases in which the effect on the ciliary body is inadequate. The important factor in fistulating operations is the iridectomy. Cyclodialysis acts directly on the ciliary body. (18 references) Ray K. Daily.

Robertson, E. Norris, Jr. **Therapy of congenital glaucoma.** A.M.A. Arch. Ophth. **54**:55-58, July, 1955.

The author believes that goniotomy is the procedure of choice in congenital glaucoma. Goniopuncture or combined goniopuncture and goniotomy may be used where goniotomy alone fails to control the tension. (4 tables, 8 references)

G. S. Tyner.

Tyner, G. S., and Swets, E. J. **Report on thirteen eyes treated by goniopuncture.** A.M.A. Arch. Ophth. **54**:59-65, July, 1955.

In a preliminary report, the authors were able to successfully lower the tension in eyes with congenital glaucoma by repeating goniopunctures several times. Although the follow-up time in all cases was relatively short, the results indicate that the procedure has merit. (1 table, 1 reference) G. S. Tyner.

Urrets-Zavalia, A., Jr., and Remonda, C. **Clinical tonography: a critical survey of the results obtained in different forms of glaucoma.** Arch. oftal. Buenos Aires **30**:89-90, Feb.-March, 1955.

After a succinct exposition of the method's foundations and of the technique employed, which was that advocated by Grant, the authors summarize the results obtained in untreated cases of acute, chronic congestive, chronic simple, congenital and secondary glaucoma, which agree consistently with those already published by others. The effect of miotic drugs, of acetazoleamide and of diverse operations on the facility of outflow are also described.

The fact that large discrepancies between the value of C and that of the I.O.P. are of common occurrence in cases of simple glaucoma is stressed and held to demonstrate 1. that the abnormally high pressure readings are only partly dependent upon an increased resistance, and 2. that, consequently, an added disturbance, probably an elevation in the uveal capillary pressure, must also come into play. This factor will have been neglected by those who identify the condition with a merely obstructive process and regard it only as the result of impaired drainage. Accordingly, the circumstance that miotics often return the I.O.P. to normal without improving C in the same proportion should not be assumed to indicate that surgery is needed. In these cases, as in those where cyclodiathermy has been successfully performed or acetazoleamide given, the eventually still progressive field loss and nerve cupping come to derive solely from the underlying, ever advancing vascular lesions, and are no longer related to the remaining obstruction or to hypothetic occasional rises of the I.O.P. to injurious levels. (1 reference)

A. Urrets-Zavalia, Jr.

10

CRYSTALLINE LENS

Goar, Everett L. **The management of monocular cataracts.** A.M.A. Arch. Ophth. **54**:73-76, July, 1955.

Unilateral cataracts should be operated upon before they reach the stage of maturity where extraction is difficult. The disadvantages of monocular aphakia can be relieved in many cases by use of contact lenses. (3 references) G. S. Tyner.

Moner Barraquer, Joaquin. **Technical improvements in the Ridley implant operation for cataract extraction.** Ann. d'ocul. **188**:364-370, April, 1955.

The author prefers to do the capsulotomy with the point of a knife, making as large a circular opening as possible, since with the capsule forceps, there is danger of rupture of the zonular fibers.

An electrically controlled rubber suction cup, applied to the center of the anterior surface of the implant, has several advantages over the use of forceps applied to its edge. There is no danger of scratching the implant. The grasp is firmer. There is less trauma to the iris.

The implant does not need to be released until it is entirely behind the iris. No movement of the hand is required at the moment of its release, since this is accomplished by the switch pedal.

Wide dilatation of the pupil is not recommended. If the pupil is not sufficiently contracted after insertion of the implant, the anterior chamber is irrigated with acetylcholine, 1:10,000, which results in immediate miosis. In addition to corneoscleral subconjunctival sutures, plasma thrombin is used to decrease the permeability of the limbal wound and to fasten the conjunctival flap. Finally, cortisone is injected subconjunctivally and eserine ointment is instilled. (5 figures)

John C. Locke.

de Saint Martin, R. **Hyphema after extraction of senile cataracts.** Arch. Soc. oftal. hispano-am. **15**:53-70, Jan., 1955.

This is a comprehensive review of the literature and an analysis of the author's material which comprises 1,613 cataract extractions without corneoscleral sutures, and 204 extractions with corneo-scleral sutures. The data show that with poor preoperative and postoperative care and in operations with conjunctival flaps and conjunctival sutures, the incidence of hyphema was 93 percent; with corneal incisions and corneo-scleral sutures, the incidence was six percent and with careful preoperative preparation, curarization, hypotonization and corneo-scleral sutures the incidence was 1.91 percent. The author's pattern of therapy, in eyes in which spontaneous absorbtion does not take place promptly, begins with daily intravenous injections of Congo red and of preparations of calcium, and diathermy locally. Under this management the hyphema usually clears within three to seven days, and if it does not, a paracentesis of the anterior chamber is performed, and the chamber is reopened daily if it refills with blood or if the removal of the clot is incomplete. The author urges that hyphema should not be accepted as a benign, unavoidable complication, and that measures to prevent it should be taken. Usually the source of hyphema is the corneal incision. Hyphema originating in the iris or ciliary body is indicative of general pathologic change such as a degenerative process, arteriosclerosis, an infection, diabetes or a dyscrasia. Ray K. Daily.

Vere, D. W., and Verel, D. **Relation between sugar level and the optical properties of the lens of the human eye.** Clin. Science **14**:183-196, 1955.

The red reflex of diabetic patients was examined with an ophthalmoscopic photometer. When the blood sugar exceeded 160 mg. per 100 ml., the brightness of the reflex was decreased and the patients complained of misty vision. When the blood sugar was normal, the brightness of the reflex was uniform. There was no change in aphakic eyes. The changes are due to a reversible opacification of the anterior band of the lens and may be related to the formation of true diabetic cataract. (11 figures, 3 tables, 14 references) Irwin E. Gaynon.

11

RETINA AND VITREOUS

Alagna, G., and Di Perri, T. **Circulatory, biochemical, and therapeutic aspects of Coats' disease.** Arch. di ottal. **59**:103-115, March-April, 1955.

In a case of bilateral Coats' disease the authors found in the photoplethysmogram of the fingers indications of a diminution of circulation time, which probably can be interpreted on the basis of a general angiopathy. The serum protein fractions were disturbed toward hypoglobulinemia; the subretinal fluid showed an identical protein distribution and an intensely positive Rivalta reaction. Small daily plasma transfusions seemed to have

a certain beneficial effect on the course of the disease. (5 figures, 17 references)
John J. Stern.

Anderson, B., and Vallotton, W. **Etiology and therapy of retinal vascular occlusions.** A.M.A. Arch. Ophth. **54**:6-12, July, 1955.

Retinal arterial occlusions from various causes were generally not amenable to treatment. Some cases of venous occlusion seemed improved by treatment. Treatment was essentially the same for both arterial and venous obstruction. Therapeutic measures are indicated before the end of the first week of arterial and the first month of venous occlusions. Treatment consists of immediate retrobulbar injection of procaine, hyaluronidase and priscoline, stellate ganglion block, and anticoagulant therapy for 30 to 60 days. Flushing doses of vasodilators and in some instances corticotropin were used concurrently. (3 tables, 9 references)
G. S. Tyner.

Bing, Ellen. **Etiology and prophylaxis of retrolental fibroplasia.** Ann. paediat. **184**:294-315, May, 1955.

The author reports a case of retrolental fibroplasia in a child who had been thoroughly and extensively studied, and makes her experience the occasion of discussing extensively the cause of the disturbance, its pathology, clinical picture, therapy, occurrence, and social implications. Current opinions are summarized and suggestions for prophylaxis are made. (30 references) F. H. Haessler.

Bischler, V., and Marty, F. **The posttraumatic chorioretinopathy of Siegrist.** Ophthalmologica **129**:231-236, April-May, 1955.

Although the lesion was originally described by J. Hutchinson Jr. in 1889, the Swiss ophthalmologist Siegrist, six years later, made the first detailed clinical study of this typical fundus lesion due to contusion of the globe and attributed it to rupture of one or several posterior ciliary arteries. The most characteristic feature of the lesion (yellowish, sharply outlined areas in the fundus which rapidly become hyperpigmented) is its presence immediately after the injury which may lead to the misinterpretation of its being an old lesion, antedating the trauma. A typical case is reported in detail. (1 figure, 12 references) Peter C. Kronfeld.

Boyd, J. T., and Hirst, K. M. **Incidence of retrolental fibroplasia in England and Wales in 1951.** Brit. M. J. **2**:83, July 9, 1955.

Member of Conference. **Retrolental fibroplasia in the United Kingdom.** A report to the medical research council. Brit. M. J. **2**:78, July 9, 1955.

In each of these two articles a statistical analysis is presented of data that had been gathered. F. H. Haessler.

Dekking, H. M. **Clinical investigation of diabetic retinopathy.** Tr. Ophth. Soc. U. Kingdom, **74**:499-501, 1954.

The author reports that in 383 diabetics of both sexes and all ages diabetic retinopathy was found in 21.6 percent, and retinitis proliferans in seven percent. Diabetic retinopathy was not related to the use of insulin or its dosage, and no correlation with glycosuria, hyperglycemia or cholesterin content of the blood, hypertension, arteriosclerosis or renal functions was found. The author did find a strong positive correlation with fragility of the skin capillaries. Rutin seems to act as a deterrent to the occurrence of petechiae as does testosterone. This effect of testosterone is to be expected as it inhibits the production of cortisone by the adrenal cortex and cortisone is known to be a factor in the development of diabetic retinopathy. (3 tables)
Beulah Cushman.

Dias, John F., Jr. **Congenital arteriovenous aneurysm of the retina.** U. S. Armed Forces M. J. **6**:908-910, June, 1955.

A case of arteriovenous aneurysm of the left eye is presented. In the fundus a very large, thick, tortuous artery was seen to come off the disc, wind around a degenerated macula, and then proceed back to the disc. The second part of this vessel is seen to be venous because of an abrupt change in color, size, thickness of wall, and pulsatile response to pressure. (1 figure, 5 references) Harry Horwich.

Glick, L., and Mumford, J. **Quinine amblyopia. Treatment by stellate ganglion block. British** M. J. **2**:94-96, July 9, 1955.

A 31-year-old married woman took 15 grams of quinine in port wine. Within a few minutes her vision was blurred. Next day complete absence of light perception, pallor of the optic discs, and narrowing of the retinal arteries were noted. After failure of the usual therapeutic measures and when the patient had been blind for 39½ hours, bilateral ganglion block was performed. The right side was done first but without benefit; only then was it learned that she had had no more than light perception in her right eye since childhood. Within one minute of completing a stellate ganglion block on the left side, the patient volunteered that she could again see. Because the initial improvement was not maintained, a stellate ganglion block was repeated daily. All treatment was stopped on the fifth day after admission. Gynecological examination gave indications for evacuation of the uterus. When a final assessment was made two months after the ingestion of the quinine, the disc was still pale, the vessels still were narrow, but edema had disappeared and the visual acuity was 6/9 in the left eye F. H. Haessler.

Jones, Barrie R. **Acute retinal periphlebitis associated with infectious mononucleosis.** Tr. Ophth. Soc. U. Kingdom **74**:119-130, 1954.

A patient, 40 years of age, lost the vision of the right eye during the course of a febrile illness. While doing some heavy lifting when back at work, the vision became blurred in the right eye. It was reduced to 6/60. In the fundus there were scattered flame-shaped hemorrhages, as in thrombosis of the central vein, and also a large subhyaloid hemorrhage. The nerve head was hyperemic and swollen. Perivascular cuffs around the inferior nasal and temporal veins suggested that the retinography was inflammatory or toxic in origin. Blood counts showed an initial leucocytosis which gave place to a mononucleosis with a significant proportion of abnormal, large lymphoid cells as in infectious mononucleosis. (8 figures, 1 table, 28 references) Beulah Cushman.

12

OPTIC NERVE AND CHIASM

Boeke, Wilhelm. **Optic neuritis in tuberculous meningitis.** Klin. Monatsbl. f. Augenh. **126**:678-684, 1955.

It was usually assumed that papilledema is a more frequent complication of a tuberculous meningitis than of optic neuritis. However, with modern methods of treating tuberculosis, the picture has changed. The author observed eight patients; six presented the picture of a papillitis and two of a retrobulbar neuritis. Most of them developed into a temporal atrophy of the disc. (18 references) Frederick C. Blodi.

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received at least three months before the date of occurrence.

Deaths

Dr. Halbert Andrew Haynes, Chicago, Illinois, died July 5, 1955, aged 84 years.

Dr. H. C. Neblett, Charlotte, North Carolina, died August 21, 1955, aged 67 years.

Announcements

Stanford spring postgraduate conference

Stanford University School of Medicine will present the annual postgraduate conference in ophthalmology, March 19 through March 23, 1956. Registration will be open to physicians who limit their practice to the treatment of diseases of the eye, or eye, ear, nose, and throat. In order to allow free discussion by members of the conference, registration will be limited to 30 physicians.

Instructors will be Dr. D. K. Pischel, Dr. Jerome W. Bettman, Dr. Max Fine, Dr. Earle H. McBain, and Dr. Arthur J. Jampolsky.

Program and further information may be obtained from the office of The Dean, Stanford University School of Medicine, 2398 Sacramento Street, San Francisco 15, California.

Mark J. Schoenberg Lecture

Dr. Georgiana Dvorak-Theobald, Oak Park, Illinois, clinical associate professor of ophthalmology and clinical pathologist emeritus, University of Illinois College of Medicine, will present The Mark J. Schoenberg Memorial Lecture on Monday, December 5th, at 8:15 P.M., at the New York Academy of Medicine. The subject of Dr. Theobald's address will be "Aqueous veins and their relation to glaucoma."

This annual lecture, sponsored jointly by the National Society for the Prevention of Blindness and the New York Society for Clinical Ophthalmology, is a memorial to the late Mark J. Schoenberg, M.D., who founded the New York Society for Clinical Ophthalmology and who was also the first chairman of the National Society's committee on glaucoma. All physicians are invited to attend.

Florida seminar

The 10th annual University of Florida Midwinter Seminar in Ophthalmology and Otolaryngology will be held at the Sans Souci Hotel in Miami Beach the week of January 16, 1956. The lectures on ophthalmology will be presented on January 16th, 17th, and 18th; those on otolaryngology on January 19th, 20th, and 21st. A midweek feature will be the midwinter convention of the Florida Society of Ophthalmology and Otolaryngology on Wednesday afternoon, January 18th to which all registrants are invited. The registrants and their wives may also attend the informal banquet at 8:00 P.M. on Wednesday. The schedule has been changed to provide a maximum time for recreation each afternoon.

The seminar lecturers on ophthalmology this year are: Dr. Francis H. Adler, Philadelphia; Dr. A. Gerard DeVoe, New York; Dr. Michael J. Hogan, San Francisco; Dr. C. Wilbur Rucker, Rochester, Minnesota; and Dr. A. D. Ruedmann, Detroit. Those lecturing on otolaryngology are: Dr. Frederick A. Figi, Rochester, Minnesota; Dr. Lewis F. Morrison, San Francisco; Dr. Charles E. Kinney, Cleveland; Dr. John R. Lindsay, Chicago; and Dr. Bernard J. McMahon, St. Louis.

Convention cruise

The Virginia Society of Ophthalmology and Otolaryngology is sponsoring a convention cruise to Havana and Nassau from May 26 to June 2, 1956. Sailing from and returning to Norfolk, Virginia, the *Queen of Bermuda* will act as the hotel for the trip. Fare for the seven days will be $165.00 and up per person. Reservations may be made through the United States Travel Agency, Inc., Washington, D.C.

Research fellowship available

A research fellowship will be available at Stanford University after the first of the year. This is open to trained ophthalmologists who wish to do some work in the various branches of research. The exact stipend will depend upon the qualifications of the individual physician. The initial appointment will be for a period of one year and, on mutual agreement, can be extended for several years. Inquiries should be addressed to Dohrmann K. Pischel, M.D., Stanford University Hospitals, Division of Ophthalmology, San Francisco 15, California.

Refresher course in eye surgery

The Faculty of Medicine of the University of Toronto offers a Refresher Course in Eye Surgery from March 26 to March 28, 1956. The guest surgeons will be: Dr. Conrad Berens, New York University; Dr. Philip Meriwether Lewis, University of Tennessee; Dr. Harold G. Scheie, University of Pennsylvania.

The instruction will consist of operative clinics

in the university teaching hospitals in the mornings and formal clinics, lectures, and case presentations in the afternoons. The staff of the Department of Ophthalmology will contribute to the course, which will be given to a minimum of 15 students with a maximum registration of 50. A fee of $35.00 will be charged, payable to the Chief Accountant, University of Toronto. Applications should be made to the Dean of the Faculty of Medicine, not later than January 31, 1956.

Societies

Dallas academy

The next meeting of the Dallas Academy of Ophthalmology and Otolaryngology will be held on Tuesday, December 6th. Mr. Jack C. Copeland, Chicago, will discuss "Streak retinoscopy," and Dr. Ralph H. Riggs of Shreveport, Louisiana, will talk on "Diagnosis in rhinoplasty."

The society's other scheduled meetings are:

Tuesday, January 3, 1956, "Fixation of facial fractures using the Kirschner wire," Dr. Herbert H. Harris, Houston; and "Technique of cataract extraction," Dr. Tullos O. Coston, Oklahoma City.

Tuesday, February 7th, a joint meeting with the Fort Worth Eye, Ear, Nose, and Throat Society. Dr. Frank B. Walsh, Baltimore, will be guest speaker and his subjects will be: "Tumors of the optic nerve and chiasm," and "Myasthenia gravis."

From March 12th to 14th the annual meeting of the Dallas Southern Clinical Society will be held. Ophthalmology guests will be Dr. Trygve Gundersen, Boston, and Dr. Jack S. Guyton, Detroit. Otolaryngology speakers will be Dr. Franz Altmann and Dr. Paul J. Moses.

Tuesday, April 3rd, Dr. Everett L. Goar, Houston, will speak on "Personal experiences in facilitating ophthalmic surgery," and "Use of contact lenses in monocular cataracts." Dr. E. King Gill, Corpus Christi, will discuss "External ear infections."

Tuesday, June 5th, Dr. Oliver W. Suehs, Austin, will discuss "Secretory otitis media," and Dr. Morton Mason, "Oxygen and the eye."

Officers of the Dallas Society are: President, Dr. Edwin G. Grafton; vice-president, Dr. L. A. Furchgott; secretary-treasurer, Dr. Hal W. Maxwell; program committee, Dr. James L. Baldwin and Dr. Albert E. Meisenbach, Jr.

Brooklyn meeting

At the 135th regular meeting of the Brooklyn Ophthalmological Society, Dr. Richard C. Troutman spoke on "Complications of cataract surgery and their management," and Dr. John M. McLean discussed "Some problems in retinal detachment."

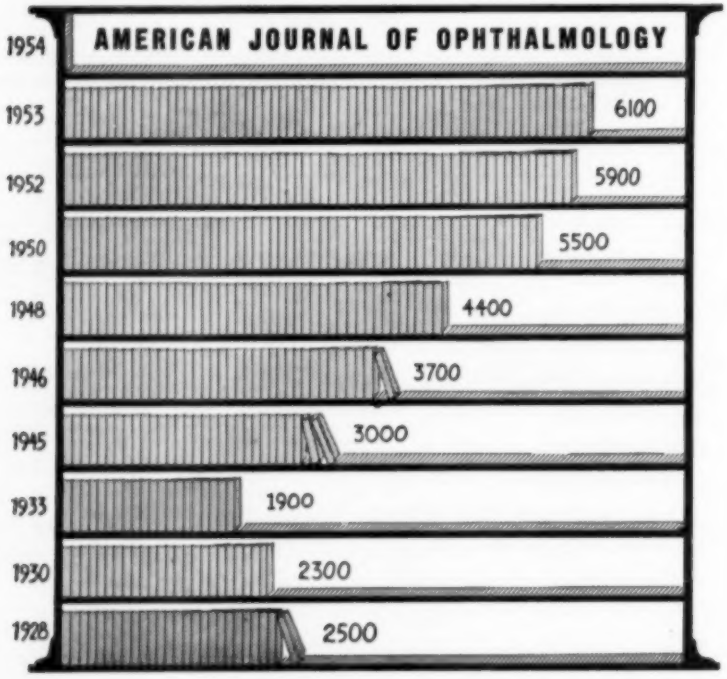
Des Moines academy

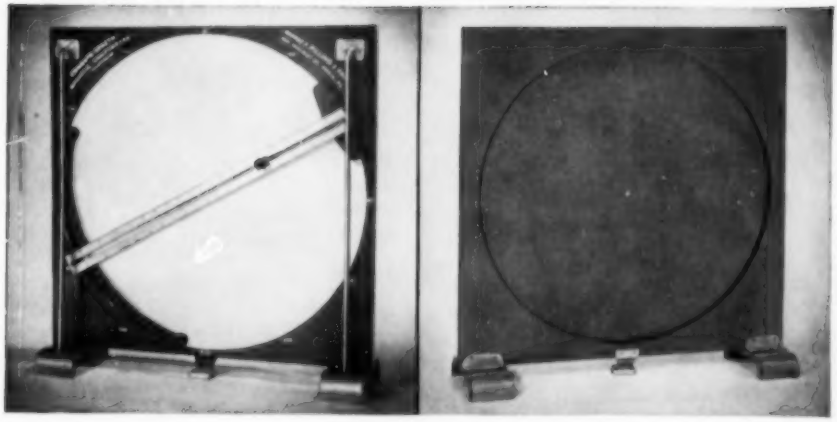
At its annual meeting the Des Moines Academy of Ophthalmology and Otolaryngology elected the following officers: President, Dr. Elmer A. Vorisek; president-elect, Dr. Robert R. Updegraff; secretary-treasurer, Dr. C. C. Walker. Meetings are held every fourth Monday, October through May.

Personals

The death of Jonas S. Friedenwald, M.D., of Baltimore, Maryland, occurred on November 6, 1955. He bore the pain of an incurable illness with fortitude. A biography of this great American ophthalmologist will appear in an early issue of The Journal.

Dr. Feliciano Palomino Dena directed the course on "Strabismus" given recently in the Department of Ophthalmology of the Children's Hospital, Mexico City, under the auspices of the Graduate School of the National University of Mexico.





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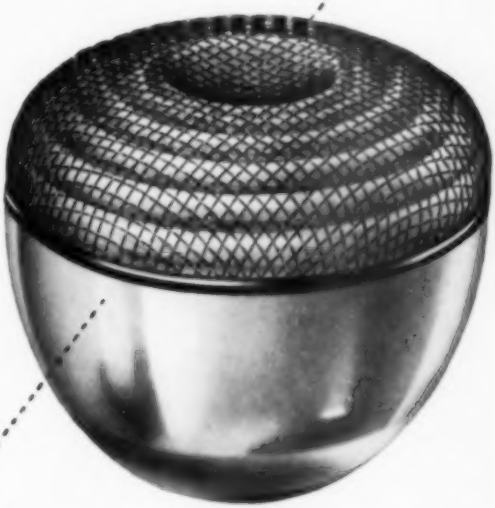

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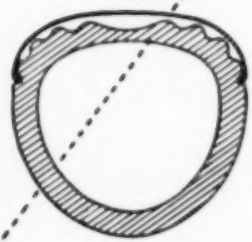

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